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THE American Journal OF Gastroenterology

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VOLUME 26 DECEMBER, 1956 NUMBER 6

A. L. LEVIN MEMORIAL LECTURE

RECENT ADVANCES IN THE ULCERATIVE DISEASES OF THE GASTROINTESTINAL TRACT*

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New York, N. Y.

In the short time at my disposal I will present to you briefly some recent advances in the ulcerative diseases of the gastrointestinal tract. Peptic esophagitis, peptic ulcer of the stomach and duodenum, regional enteritis, diffuse jejunoileitis and ulcerative colitis will be discussed.

First let us discuss *peptic esophagitis*. Of historical interest is the following: —before 1934, numerous papers had appeared in the literature describing the solitary peptic ulcer of the esophagus. In 1934, I gave a paper at the American Medical Association Meeting in Cleveland entitled "Peptic Esophagitis—A New Clinical Entity". I described at that time reflux esophagitis associated with duodenal ulcer, rarely with gastric ulcer and even more rarely with esophageal ulcer. In the 1940's Allison, a surgeon in England, described marginal or reflux esophagitis adjacent to sliding esophageal hiatus herniae. Later, in the early 1950's, Barrett, also in England, described solitary peptic ulcer and stated that it occurred in an esophagus which was lined with ectopic gastric mucosa.

The chief symptoms of peptic esophagitis are heartburn, pain, dysphagia, anemia, loss of weight, stenosis, and hemorrhage. Medical antiulcer therapy and surgical therapy including repair of the herniae and esophagogastrectomy for the severe cases, are usually curative in these conditions. The classification of these cases in separate groups has constituted a major advance in recent years.

There are other groups of esophagitis due to prolonged vomiting, prolonged esophageal intubation, and also, after anastomotic operations.

*Read before the Southern Regional Meeting of the American College of Gastroenterology, New Orleans, La., 8 April 1956.

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The second subject which we will discuss briefly is that of *gastric and duodenal peptic ulcer*. We will consider here chiefly the etiology and therapy. The ultimate cause of this disease is probably an emotional disturbance in the psychologic unconscious. We recently observed a young colored girl with a huge gastric fistula which resulted from a suicidal attempt with lye. The lye led to a complete stricture of the esophagus, necessitating a gastrostomy. During certain psychoanalytic situations the various functions of her stomach, as studied by the physiologist, became dissociated. For example:—motility decreased and secretion increased. This is an abnormal condition. Obviously, such states, if chronic, could lead to ulceration.

The immediate cause of peptic ulcer is a prolonged basal hypersecretion in the empty stomach digesting away a mucosa made susceptible by certain causes in certain sites. Usually these sites are the lesser curvature, prepyloric region and the duodenal bulb.

During the past two years, Drs. Druckerman, Bryer, Hollander and I, have instituted a new surgical preparation in dogs for the production of experimental duodenal ulcer. An esophagojejunostomy is performed leaving the stomach in continuity with the duodenum and preserving carefully its entire vagal and vascular supply. Such a preparation in dogs who were fed frequently, at least four times daily, led to chronic duodenal ulceration in five of eight dogs. This suggests a mechanism analogous to what many observers believe exists in human ulcer patients, namely, a continuous acid secretion with hypermotility in the empty or fasting stomach. This tends to confirm the acid theory of ulcers. We are now studying carefully further experiments on the mechanism, therapy and prevention of these ulcerations. Certainly, these experiments support the idea that one of the most important attacks in the problem of ulcer therapy should be directed against the acid-pepsin factor.

The advances in the therapy of peptic ulcer are as follows:—psychotherapy, including psychoanalysis, may be used in properly selected cases; the continuous intragastric therapy using milk or alumina-gels which has proved since its introduction by me in 1929, to be the only method of controlling night secretion; anticholinergic drugs, such as Pro-Banthine, Prantal, Pamine, and so forth, plus a tranquilizing drug, such as Serpasil, seems of great value. Since these alone do not control the acid, it is necessary to add Phosphaljel or some other long-acting, nonabsorbable alkali. We have found that a combination of Prantal, Serpasil and Phosphaljel with a liberal ulcer diet is highly efficacious in the therapy of uncomplicated gastric and duodenal ulcer.

Sustagen:—Recently Sustagen, a liquid nutriment for the purpose of improving patients postoperatively and in debilitated states, has appeared. The idea occurred to me that this liquid nutriment, which is high in protein and carbohydrates, low in fat and has an adequate vitamin and mineral content, should be an ideal ulcer remedy. We tested its neutralizing properties and

found the following: a glass of Sustagen, 180 c.c., will control the free hydrochloric acid for fully two hours in 95 per cent of the cases. Following a glass of milk, however, 180 c.c., the stomach shows a considerable amount of free acid within the next 2 hours. In 40 per cent of the cases the acidity was even higher than during the fasting period.

Sustagen lends itself readily not only to oral intake but to drip therapy. To date we have treated a large series of cases with Sustagen by mouth in the daytime and by drip therapy during the night. We have been impressed by the rapid loss of symptoms and prompt healing, in cases refractory to other therapies. We advocate, therefore, strongly, a trial of this method of therapy.

Nulacin:—Douthwaite in England, following my idea of drip therapy, decided to try the incorporation in lozenges of Horlick's malted milk, soluble antacids, such as magnesia carbonate and magnesia oxide. His idea was that such a lozenge, held between the cheek and the teeth, slowly dissolving drop by drop, could really constitute an ambulatory drip therapy and continuously neutralize the interdigestive acid secretion. Douthwaite and Hunt found that this sort of tablet definitely does neutralize the acid gastric secretion. In recent experiments with placebos we have found an increased acidity following the placebo but a complete neutralization during the half hour in which the tablet containing the alkali is in the mouth. We think that this type of therapy is of great value in the control of acid symptoms, such as heartburn, sour belching, and sour mouth and even ulcer pain.

Carbamine:—Another form of ulcer therapy recently introduced is Carbamine. Carbamine is a mixture of an effervescent powder and urea. The basic idea is to supply the enzyme of the surface epithelium of the stomach, urease, with a large amount of its substrate, urea, and the enzyme carbonic anhydrase in the parietal cells with a large amount of its substrate, carbonic acid. It seems theoretically probable that this will improve the cellular function. I have treated 60 cases with this effervescent mixture. A level teaspoonful in a half glass of water four times a day between the meals is the usual dosage. The symptomatic results have been very good in these 60 cases. We are now studying the effect of this substance on acidity, pepsin, mucus and the radiographic picture.

We will next discuss the surgical therapy of peptic ulcer. Our experience with vagotomy is as follows:—when vagotomy is used alone, in the therapy of duodenal ulcer, the results have been poor. The ulcer has not healed in a fair per cent of cases and the motor disturbances have been very distressing. We feel, however, that for recurrent jejunal ulcer after gastroenterostomy or partial gastrectomy, it is worthy of a trial, although it is not universally successful. In poor-risk duodenal ulcer patients, bilateral subphrenic vagotomy combined with gastroenterostomy is a fairly successful operation. In patients with severe duodenal ulcer with very marked hypersecretion and a history of hemorrhage, bilateral vagotomy combined with subtotal gastrectomy is an operation of great

value. In this latter group of patients, recurrences have practically not been seen. The achlorhydria following this operation occurs in a high percentage of cases, 90 per cent, as compared with 65 per cent in those who have a subtotal gastrectomy alone without the vagotomy.

We will next discuss *regional enteritis*. If one bears this disease entity constantly in mind and employs good radiographic studies of the small bowel, numerous cases of this disease will be uncovered. As a matter of fact, since the first description in 1931, we have seen over 600 cases at The Mount Sinai Hospital.

The etiology of this disease is unknown. Some consider it a psychogenic disease. Granulomatous stenosis and internal and external fistula formation, are characteristic and differentiate it from nonspecific ulcerative colitis where the lesion is chiefly mucosal rather than submucosal. No form of medical therapy heals. Surgically, side-tracking without resection, if done in the fibrotic, healing stage, is curative in at least 75 per cent of the patients. Surgical therapy should not be instituted too early, that is, in the superficial ulcerative stage, since this is frequently followed by recurrences proximal to the anastomotic site. Rarely is this disease combined with ulcerative colitis.

We will next consider briefly *diffuse jejunoileitis* which pathologically resembles regional enteritis very closely. In fact, some authorities have stated that they feel that these diseases, viz, regional enteritis, diffuse jejunoileitis and ulcerative colitis are unitary diseases with a unitary etiology. In diffuse jejunoileitis, alternate diseased strictured areas and healthy areas are seen. The healthy areas prevent a sprue picture.

In this disease, also, there is no known medical cure. Surgical extirpation is hazardous because of the wide extent of the disease, and when performed may lead to dangerous deficiency states. Spontaneous improvement has been noted but not complete healing. The disease may go on for many years or the patients may succumb rapidly to toxemia or obstruction.

We will next consider briefly "nonspecific" or "indeterminate" *ulcerative colitis*. The number of cases in the United States seems to be increasing. We see approximately 300 cases a year in our hospital. The geographical incidence is of interest. It seems quite rare in South America, Italy, Spain and Portugal, despite the presence in these countries of numerous parasitic and infectious dysenteries.

Today, it is generally considered that the etiology is a psychogenic one. The function which is chiefly disturbed in this seems to be the vascular function. Recently we studied a patient with ulcerative colitis, who because of an apparent lower colon obstruction, had a cecostomy. This exposed to observation the entire mucosa of the cecum and ascending colon. Under certain psychoanalytic situations involving chiefly anger and resentment, the mucosa became very

hyperemic and petechial hemorrhages appeared. The other colonic functions, motor and secretory, were not upset. This probably represents another example of dissociation of an organ's functions through disordered stimuli arising in the psychologic unconscious.

We have also noticed in all types of ulcerative colitis whether mild, severe, acute or during a remission after a successful operation, a marked peripheral vasoconstriction when the patients were studied with plethysmography. This disturbance in the vascular function should lead to some interesting studies in the etiology and therapy of this disease. Secondary infection of the disturbed mucosa by viruses and bacteria assumes considerable importance.

Some of the advances in medical therapy of ulcerative colitis include: 1. the psychiatric approach, both superficial and deep psychotherapy; 2. the use of corticotropin and cortisone seems of great value in lessening the inflammatory reaction. Of special value in our experience in the past few years has been Meticorten. Despite the claims that this may produce ulcer symptoms or cause an exacerbation of a latent ulcer, we have not observed this in our patients who have been on Meticorten therapy for over six months. A study of the gastric secretion in these cases with prolonged Meticorten therapy has not revealed any increase in gastric secretion either in volume or acidity.

Remissions, not cures, are seen frequently with this form of therapy. That antibiotics, sulfathaladine, and transfusions are of value is quite evident. We have over a span of several years tried complete parenteral feeding for periods of several days. One or two such periods of treatment often leads to a dramatic remission.

The surgical therapy of ulcerative colitis is imperative for massive hemorrhage, pseudopolyposis, intractability and suspected carcinomatous degeneration. With reference to carcinoma in this disease, all observers agree that irrespective of age or the presence or absence of inflammatory polypi, ulcerative colitis, which exists continuously for more than ten years leads frequently to colonic carcinoma. The indication for surgical therapy is more pressing, therefore, in the patients with a long, continuous history of the disease. We are now in favor of ileostomy with simultaneous subtotal colectomy and later abdominoperineal resection of the rectum and the remainder of the sigmoid. Patients with ileostomy and total colectomy may lead a completely normal life.

MASSIVE UPPER GASTROINTESTINAL HEMORRHAGE
A SURVEY OF 253 RECORDS*

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and

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New Orleans, La.

A survey of the records of patients admitted to Touro Infirmary, New Orleans, because of copious bleeding from the upper gastrointestinal tract showed that 253 patients were treated for this symptom during the calendar years 1952-1955. All were admitted solely because of massive hemorrhage or developed it while hospitalized for other reasons. Ninety-five per cent of the patients were treated by private physicians and surgeons and five per cent were patients in the public wards. It is evident that no single plan of treatment or team could be used to treat this series of patients. Nevertheless, a decided trend to consider the advent of hemorrhage as a surgical complication by the internists was noted and early requests for surgical opinions were the rule rather than the exception. On the other hand, 18 per cent of the 253 patients who were admitted directly to surgical services were allowed to recover without operative procedures.

Selection of Patients

Hematemesis, melena or both were considered massive when the hospital records showed reasonable evidence that more than a pint of blood was lost. Syncopal episodes that were associated with melenic stools, of tarry color, were considered as strong evidence that profuse bleeding had occurred, while some who fainted after seeing brown vomitus were discarded, because there was no convincing evidence that the syncope was not due entirely to the sudden realization that the material vomited was blood and not to the quantity of blood lost. Also discarded were patients complaining of melenic stools of mild to moderate amount that were easily recognized as fresh and recently clotted blood, not preceded by tarry stools, because the bleeding lesion was probably in the lower gastrointestinal tract.

Age and Sex Incidence

All were white patients. Table I illustrates the distribution according to age and sex. There were 80 per cent (204) males and 20 per cent (49) females,

*Read before the Southern Regional Meeting of the American College of Gastroenterology, New Orleans, La., 8 April 1956.

From the Department of Surgery, Louisiana State University School of Medicine and Touro Infirmary, New Orleans, La.

†Senior Resident in Surgery at Touro Infirmary.

a ratio of 4:1. The youngest was seven years and the oldest 86 years. One and six-tenths per cent were under 21 years; 20.1 per cent were 21 to 40 years; 52.6 per cent were 41 to 60 years; and 25.7 per cent were 61 to 86 years. Seventy-eight per cent were over 40.

Location of the Lesion

Table II shows the grouping of the 253 patients into eight categories according to nature and location of the offending lesion, as noted on the hospital record at the termination of hospitalization. Definite lesions were located in 94.9 per cent by radiology, surgery, esophagoscopy, gastroscopy and studies of specimens removed at surgery.

One hundred forty-six (60.8 per cent) entered the hospital having lesions above the ligament of Treitz or cirrhosis of the liver that had been found

TABLE I

Age and Sex Distribution of 253 Patients

Touro Infirmary

Age	Male	Female	Total	Per cent
0-20	0	4	4	1.6
21-40	43	8	51	20.1
41-60	112	21	133	52.6
61-86	49	16	65	25.7
	204	49	253	100.0

before bleeding occurred. It does not follow that these known lesions were always producing the hemorrhage, nevertheless they must be regarded as the culprits until proved innocent. One hundred seven had had no diagnoses made in the past of diseases of the upper gastrointestinal tract or of the liver, so they presented diagnostic as well as therapeutic problems. The presence of hematemesis in 46 narrowed the search to the gastrointestinal tract above the ligament of Treitz and definite lesions were found in 44 while in 2 no causative lesion could be identified.

Tarry melena without hematemesis was encountered in 61 patients. This group accounted for 11 of the patients classified as having hemorrhage of undetermined cause. Stone[1], Rives and Emmett[2], Quinn and Ochsner[3] have called attention to the difficulties encountered in localizing bleeding from lesions so situated that only melena occurs and also, to the frequency of bleed-

ing from colonic diverticulosis and rectosigmoid lesions. Forty-one patients with melena complained of mild to severe pain in the epigastric region of the abdomen, which became more severe just before hemorrhage was noted, and subsided shortly after the onset of bleeding. This type of history is always helpful and it proved to be so in this series. The remaining 20, with no symptoms except bleeding, produced the eleven undiagnosed lesions.

Early x-ray examinations, within 48 hours after entering the hospital, were done 19 times with 9 positive diagnoses made within the first 24 hours and 9

TABLE II

SOURCE OF HEMORRHAGE 253 PATIENTS

TOURO INFIRMARY

Organ and Disease	Number	Per cent	Male	Female
Duodenal ulcer	145	57.3	125	20
Gastric ulcer	36	14.2	24	12
Gastrojejunal ulcer	6	2.7	5	1
Esophageal varices	36	14.2	31	5
Gastritis	9	3.5	6	3
Gastric carcinoma	4	1.5	3	1
Miscellaneous	4	1.5	4	0
Undetermined	13	5.1	6	7
	253	100.0	204	49
			80.6%	19.4%

positive and one questionable diagnosis in the second 24 hours. In only one instance was it noted that the examination might have caused recurrence of bleeding. The early use of x-ray[4,5,6] examinations is contraindicated only when shock is severe.

The double-balloon triple-lumen Sengstaken-Blakemore tube was not used for diagnostic purposes[7]. That and the single-balloon triple-lumen tube reported by Nachlas[8] are safe and valuable diagnostic instruments to differentiate esophageal from gastric bleeding and have the advantage of therapeutic value[9] when the esophagus is the source of hemorrhage. Liver function tests are valu-

able assets, but require too much time to be of value during profuse bleeding. The bromsulfalein retention determinations were the most consistent of the liver function tests in this series.

The associated diseases most commonly found were diaphragmatic hernia 23 patients, hypertension 9, diverticulosis of the colon 8 (barium enemas were not used in every case), cardiac diseases 7, cholelithiasis 4, carcinomas outside of the gastrointestinal tract 4, and diabetes mellitus 3. Two peptic ulcers were present in patients who bled from esophageal varices. Three instances of gastric and duodenal ulcers occurring in the same patient were noted.

Shock and Blood Replacement

The acute shock that accompanies massive hemorrhage is primarily dependent upon how rapidly and how profusely blood is being lost. There are, however, other important factors that are significant; such as, the patient's

TABLE III

Blood Replacement Medical and Surgical

Age Group	Surgical Average No. Units Used	Medical Average No. Units Used
41-60	5.5	2.4
61-84	7.9	4.0

response to bleeding, his age, and the presence of chronic debilitating diseases. The youthful patient can be deceptive because of his labile compensatory mechanism especially when recumbent, and may show no outward signs of shock until his blood volume has reached a dangerously low level.

The absence of acute shock does not mean that the quantity of blood lost has not been of massive proportions. Sixteen patients who complained only of weakness, dizziness, feeling faint and episodes of tarry stools for from 4 to 21 days, had red cell counts below 3 million and hematocrit readings below 20 per cent.

Blood volume determinations by the I^{131} method were valuable in estimating the amount of blood lost to the circulation because of accuracy and the minimum time required to obtain the estimate. It was useful when the patient was first seen and also for checking the results of the therapeutic measures taken to restore blood volume.

Rapid loss of blood was noted for nearly all of the 36 patients with esophageal varices and consequently, severe shock commonly accompanied the hemorrhage. The average blood replacement per patient was 3,500 c.c. while

those who required surgery averaged 6,000 c.c. per patient. All members of this group were over 40 years. Table III shows the average amount of blood per patient for lesions of the stomach, duodenum and jejunum treated medically and surgically according to age groups. Those whose ages were between 61 and 86 required almost twice the quantity needed for the 41 to 60-year group.

Medical Treatment

One hundred and seventy (67 per cent) of the 253 patients received medical treatment only. Thirty had portal cirrhosis complicated by bleeding esophageal varices. Three of these had brief severe episodes, but did not bleed after entering the hospital, so transfusions were not necessary. Seventeen continued to bleed after admission, two requiring the Sengstaken-Blakemore tube, but stopped spontaneously with adequate medical care and blood replacement. Ten patients (33 per cent) died from hemorrhage and/or liver coma.

TABLE IV

Medical Deaths

Age	Lesion	Cause	Associated Disease
63	Gastric Ulcer	Hemorrhage	Carcinoma of Prostate
64	Duodenal Ulcer	Hemorrhage	Carcinoma of Ureter
77	Gastric Ulcer	Hemorrhage	Myocardial Infarct

Mortality 2.1%

One hundred forty treated medically had massive hemorrhages from the stomach, duodenum and upper jejunum. Twenty-three of these had moderate blood loss and showed mild to no shock when admitted to the hospital. All recovered after the administration of 5 per cent glucose in distilled water as intravenous infusions and gave no evidence of further bleeding. Sixteen others gave histories of bleeding, melena with or without occasional moderate hematemesis occurring during periods of from 4 days to more than three weeks. Their red blood cell count varied from 1.9 million to 3.9 million (average 2.8 million) with total leucocyte count between 4,900 and 18,200. All were amenable to well spaced blood transfusions and proper dietary measures. One hundred and one patients had histories of more recent onsets of moderate to severe hematemesis and/or melena and were in mild to severe shock when first seen. Eighty-four continued to bleed after treatment was started but showed no dangerous signs of recurring shock, except for 11 in the 61 to 86 age group. These elderly patients showed persistent tendencies to continue bleeding and to return to shock levels. Eight had duodenal ulcers, 7 of whom recovered, but

required 2,500 c.c. to 5,000 c.c. of whole blood, while the patient who died was given 7,500 c.c. Two gastric ulcer patients who died were each given 3,500 c.c. of blood. The remaining patient had a marginal ulcer and recovered after blood transfusions amounting to 3,500 c.c. were given. The average duration of hospitalization for all patients treated medically was 13 days. There were three deaths from massive hemorrhage from peptic ulcers, two also had advanced cancer of the urinary tract. The mortality rate is 2.1 per cent. When the ten deaths from esophageal hemorrhage are added the total number of deaths is 13, or 7.6 per cent of 170 patients (Table IV).

Surgical Treatment

The 83 patients operated upon for massive hemorrhage can be divided into three groups according to the time relationship of the operation to the active bleeding as follows:

TABLE V

Surgical Deaths

Age	Lesion	Cause	Associated Disease
49	Gastrojejunal Ulcer	Thrombosis of Aorta	
59	Gastric Ulcer	Cardiac	Aortic aneurysm
64	Duodenal Ulcer	Intestinal Obstruction	
82	Gastric Carcinoma	Hemorrhage	

Mortality 5.2%

1. Emergency surgery during active bleeding:—Thirty-eight were operated upon to arrest hemorrhage who had failed to respond to medical treatment and repeated blood transfusions. All were life-saving measures taken to staunch the flow of blood. Thirty-two recovered and six died. Two of the six who died were patients with portal cirrhosis who were bleeding from esophageal varices. One death followed splenectomy and the other followed gastrotomy and ligation of the left gastric artery. The third death followed subtotal gastric resection with vagotomy for bleeding marginal ulcer. The fourth death followed subtotal gastric resection for a posterior gastric ulcer that had perforated and caused erosion of the splenic artery. The fifth death followed a blind subtotal gastric resection. At autopsy the cause of the hemorrhage was found to be a duodenal ulcer. The sixth patient who died had had a subtotal gastric resection for carcinoma of the antral portion of the stomach; death resulted from postoperative hemorrhage.

The mortality for the 38 emergency operations is 15.7 per cent.

2. *Semiemergencies:*—Twenty-six patients who had frequent hemorrhages before the current hospitalization were referred to surgery after bleeding had stopped and blood volume elevated to normal levels by blood transfusions and supportive measures, thus the urgency that accompanies emergency surgery was removed. The patients were better able to withstand definitive surgery and added procedures that might be found necessary by abdominal exploration.

There were no deaths following surgery in this group.

TABLE VI

DEATHS AND MORTALITY RATE

Source	Total Treated	Deaths	Per cent Mortality
Duodenal Ulcers	145	2	1.4
Gastric Ulcers	36	3	8.3
Gastrojejunal Ulcer	6	1	18.0
Esophageal Diseases	36	12	33.3
Gastritis	9	0	0.0
Gastric Carcinoma	4	1	25.0
Miscellaneous	4	0	0.0
Undetermined	13	0	0.0
	253	19	

Total Mortality 7.5%

3. *Interval Surgery:*—Nineteen patients who recovered from massive hemorrhages were discharged from the hospital and after several weeks of medical treatment were re-admitted for surgery. These were in 17 instances patients with ulcers that resisted medical treatment and had had several episodes of massive hemorrhage. Here again definitive surgery could be carried out with greater safety to the patient. The two exceptions were patients who had had gastrotomies and suture ligatures applied to bleeding arteries as emergency procedures and had returned for definitive surgery.

There were no deaths in this group.

The operation of choice for peptic ulcer was subtotal gastric resection, usually without vagotomy. Gastrotomy was used frequently to locate the bleeding lesion and was usually followed by gastric resection. Exploration of the lower esophagus through gastrotomy incisions with a finger or a tightly folded sponge located the bleeding lesion on two occasions. The Sengstaken-Blakemore tube was immediately inserted in one. Total gastric resection and splenectomy was done once for a gastric lymphosarcoma that was the source of the hemorrhage.

The most frequent complication encountered was, ironically, postoperative hemorrhage. There were seven patients who bled after surgery with one death. Two spleens that were injured during the process of mobilizing the stomach had to be removed. The average postoperative hospitalization period for surgical patients was 12 days. There were four deaths following operations for lesions of the stomach, duodenum and jejunum in 77 patients giving surgery a mortality rate of 5.1 per cent for the peptic ulcer group. When 2 deaths resulting from surgery for esophageal hemorrhage are added the mortality for the entire group (83) becomes 7.2 per cent (Table V).

Of the 253 patients, 19 died—total mortality 7.5 per cent (Table VI).

Discussion

Seventy-nine per cent of the patients reported here stopped bleeding without operative measures. Twenty-one per cent apparently would not, so they were submitted for direct attack upon the lesion. They were patients with active and copious bleeding that showed no signs of abating with adequate blood replacement; therefore, they were truly candidates for attempts at surgical arrest. There can be no contraindication to surgical arrest of bleeding in such a situation because bleeding from the vessels in and immediately adjacent to the gastrointestinal tract follows the same course as bleeding from any other part of the body and the shock that accompanies it is just as deadly.

When called upon to treat a patient with massive hemorrhage, it is the duty of the surgeon to place his primary mission, the arrest of hemorrhage, above everything else. A concerted effort must be made to find the site of bleeding and when gastric resection does not remove the lesion the bleeding vessels must be secured. Definitive treatment for the disease, when it can be safely accomplished, must be considered a "bonus" and not a "must", for frequently, it is safer for the patient if we leave the resection for a later day. We stress the suture ligation of the bleeding vessels, because a great number of duodenal ulcers cannot be removed for technical reasons and may continue to bleed postoperatively.

Finally, age and associated diseases should not delay surgery that is urgently needed because such patients usually tolerate early operations much

better than they do mounting blood loss and shock. The fact that the bleeding is occurring for the first time does not alter the situation because most deaths in this series (14 of 19) occurred with first hemorrhages.

Conclusions

1. A study of the records of 253 patients with massive upper gastrointestinal hemorrhage is presented.

2. Seventy-nine per cent of the patients had spontaneous arrest of bleeding.

3. Patients who have had one or more episodes of massive bleeding, not caused by blood dyscrasias, are candidates for interval surgery to avoid recurrences.

4. Definitive subtotal gastrectomy is more safely accomplished as an interval procedure.

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THE PROBLEM OF NONSPECIFIC ULCERATIVE COLITIS IN THE NEW ORLEANS AREA*

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Since the title of this presentation suggests a special individuality of the disease "Idiopathic Ulcerative Colitis" as it occurs in the New Orleans Area, it is necessary to delineate clearly the nature of the disease to be discussed under this title. Synonymous terms include "thromboulcerative colitis", "colitis gravis", "nonspecific ulcerative colitis", and "chronic suppurative colitis". A basic concept of ulcerative colitis is that it is a disease *sui generis*: hence the many instances of ulcerative processes involving the colon for which specific causes can be demonstrated—*Endameba histolytica* and *Shigella* infections, mercury poisoning and lymphogranuloma venereum, among others—are eliminated. Only for those instances of ulcerative colitis where no specific etiologic agent can be demonstrated is the term "nonspecific ulcerative colitis" reserved.

Often regional enteritis (cicatrizing enterocolitis), "right-sided colitis" and "segmental colitis" are lumped together with nonspecific ulcerative colitis under the latter term without much clinical or pathological justification. The point of confusion seems to arise from the fact that in some 15 to 20 per cent of the examples of regional enteritis (cicatrizing enteritis and enterocolitis) the colon is involved also, and in about 30 per cent of cases of nonspecific ulcerative colitis the distal ileum is involved. This overlap in the region of the ileocecal valve appears to be the basis for this confusion. Yet on clinical and on pathologic evidence the two may be differentiated in almost every instance[1].

Regional enteritis (cicatrizing enteritis and enterocolitis) with its sharply demarcated areas of involvement, its "skip areas", its tendency to spread proximally in the small intestine and distally in the large intestine, and its infrequent involvement of the sigmoid and rectum is distinctive. On the other hand nonspecific ulcerative colitis characteristically involves colonic segments in a continuous fashion and does not exhibit sharp discontinuities. The disease spreads from the almost invariably involved distal sigmoid and rectum proximally toward the cecum and often extends into the terminal ileum. The basic pathologic lesion of regional enterocolitis is a progressive granulomatous submucosal lymphangitis[2] with secondary stercoral ulceration. In ulcerative colitis the involvement is in the superficial layers of the mucosa. Small crypt abscesses occurring in crops are characteristic. These minute lesions result in hyperemia, edema

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and ulceration of the colonic mucosa. Eventually hyperplastic pseudopolypoid and fibrotic chronic changes occur in the bowel wall. These considerations eliminate from this discussion subjects with "segmental colitis", "right-sided colitis" or "enterocolitis".

Prevalence and Geographic Distribution of Ulcerative Colitis

Nonspecific ulcerative colitis is world-wide in its distribution, but its known incidence is low. It is believed to be more common in some localities than in others. Bockus[3] indicates that the disease is less common in the South than in the North, and Kirsner and Palmer[4] believe it to be less common in temperate South America than in North America. Despite these interesting speculations there are few data upon which reliable estimates either of the general prevalence of the disease or its relative frequency of occurrence in different localities can be based. As indirect evidence which suggests the less frequent occurrence of ulcerative colitis in the Southern States, the paucity of clinical reports on the

TABLE I

Institution	Period Observed	Total Admissions	Nonspecific Ulcerative Colitis	Rate/1000
Touro, New Orleans, La.[12]	1951-1955	99,989	104	1.04*
Charity Hospital, New Orleans, La.	1952-1955	277,609	79	0.3
Veterans Administration Hospital, New Orleans, La.	1946-1956	51,297	42	0.8

*These are maximal figures. Each readmission of a patient appears in this compilation as a new patient for the year concerned[12].

disease which originate from Southern centers may be cited. While much of the data do not permit actual rate calculations, the number of instances of the disease reported from certain other areas is apparently much larger than could be accumulated in the New Orleans Area, at least, in a comparable period of time.

Spriggs[5] reported from England a rate of about 5 per thousand admissions to general hospitals, and Kantor[6] estimated about 9 per thousand private patients with intestinal complaints in New York. The report of Sloan and his associates[7] in 1950 involved data derived from a review of the records of 2,000 patients with nonspecific ulcerative colitis admitted to the Mayo Clinic between the years 1918 and 1937. It was stated in this report that most of these patients came from the middle west. Kirsner and Palmer[4] from Chicago report on 120 patients presumably seen within a relatively short period of time. As a basis for comparison I have tabulated the number of patients recorded in three New

Orleans hospitals as having nonspecific ulcerative colitis and have calculated the rate from the total number of discharges during the time in question. These data are presented in Table I.

They suggest that the prevalence of ulcerative colitis in fact may be less in the New Orleans Area than in more northern latitudes. There are a few other studies which document regional variations in the rate of occurrence of ulcerative colitis. One of these, a recent study from Great Britain[8], indicates that the disorder is less common in Scotland than in South England. In this study the over-all rate in Great Britain for the hospitals studied was 1.1/1000 general admissions.

Etiologic Considerations

Geographic variations in the prevalence or manifestations of disease occasionally furnish valuable clues to etiology. Can any such significance be attached to the diminished incidence of ulcerative colitis in New Orleans? Suggested, of course, is the fact that special types of infection related to geographical location may be of importance in the etiology of ulcerative colitis. Among these infections is shigellosis. Felsen[9], for example, was an ardent advocate of the proposition that nonspecific ulcerative colitis is a special chronic form of bacillary dysentery. There is, however, no reason to believe that infection with enteric pathogens is less common in New Orleans than in areas where ulcerative colitis is more common. Similar evidence on this score was presented by Melrose[8] who found that the incidence of shigellosis was higher and the incidence of ulcerative colitis lower in Scotland than in South England where shigellosis was less and ulcerative colitis more frequent.

Infection with *E. histolytica* has been suspected of being an important antecedent infection in some patients with ulcerative colitis. Surely infection with this parasite is more common in New Orleans than in the latitudes of the United States where ulcerative colitis is more prevalent. It is true that in certain neglected patients with amebic colitis, the colon may eventually show hyperplastic mucosal changes together with a thickened fibrotic wall. This nonfunctional tube is very similar to that seen in nonspecific ulcerative colitis, and differs mainly in the fact that *E. histolytica* is present in bowel exudate and in the tissue. Such a patient is exemplified by the following:

A 61-year old man had had intermittent bloody diarrhea for "years". His chronic asthma had been repeatedly treated but the dysentery had received little attention. Gross bleeding brought him to the hospital where he died a few hours after admission from an exsanguinating hemorrhage and shock. *E. histolytica* was found in the bowel exudate and in the walls of the colon and terminal ileum. The colon was a nonfunctional hyperplastic and fibrotic tube. The appearance of this colon was not unlike that seen in chronic non-

specific ulcerative colitis, but the presence of *E. histolytica* in the tissues and bowel exudate precluded this diagnosis.

There appears to be a parallelism between the geographical distribution of ulcerative colitis and rheumatic fever as indicated in studies by the Seegals and their associates[10,11] and the generalizations offered above about the distribution of ulcerative colitis. Since rheumatic fever is generally acceded to be a response to infection with the hemolytic streptococcus, the similar geographic distribution suggests that this organism may be important in the causation of ulcerative colitis. Extensive studies[10,11], however, showed that there is no diminution of streptococcal infections to account for the diminished prevalence of rheumatic fever and, by analogy, ulcerative colitis in Southern localities.

My own experience with nonspecific ulcerative colitis in New Orleans has included the study of 72 patients in various institutions. With few exceptions psychosomatic factors seem to be present and constitute an important consideration in most of these individuals. This is in contradistinction to the findings reported by Sloan et al[7] who rarely found such association. They placed much stress on distinct psychically traumatizing events as important factors. While such traumas are important trigger devices for recurrent episodes, the basic problem lies much deeper than this. Deep-seated personality problems are usually the rule. A characteristic failure of accomplishment seems to be the recurrent pattern in many of these patients, and in most instances, it is established long before the symptoms of colitis begin and frequently it can be traced from childhood. These subjects continue to utilize childish devices to avoid the stresses of responsible adults. Often these individuals are unwilling to assume any of the responsibility for getting well and bring a rebellious, aggressive hostility, lightly disguised, into the doctor-patient relationship. As an example of the type of psychosomatic problem which is important, the following is cited:

A 25-year old man is the younger of two children. His older sister was always a leader in school and extracurricular activities. Whenever the patient attended schools in which his sister had preceded him, her rather brilliant record was cited as an example of how well he should do. He responded to the challenge with dismal failures. He was successful only when he attended institutions where his sister was unknown. When the patient was 13 years old his father died of cancer of the colon. His mother's remarriage, slightly more than a year later, has never been accepted by the patient as other than an iniquitous act of desertion. He soon became incorrigible. Placed in a military school, he ran away frequently, set fire to buildings and committed other acts of destructive nature. These acts required much attention from his mother and stepfather and the patient relates these escapades with savor. After finishing a public high school he "flunked out" of a university at the time of the first examinations. Following a period of Army service he attempted to attend another uni-

versity. He was unable to take the examinations because he had become ill with intractable diarrhea which forced him to quit the school. A second period of Army service was a happy experience until he was sent to a leadership school. The prospect of responsibility terrified him and he requested that he be returned to his former duties when he found that he had to direct the activities of other people. Immediately following this episode he developed intractable bloody diarrhea, anemia, fever and weight loss and was discharged from the service with a diagnosis of nonspecific ulcerative colitis.

He has been hospitalized four times since 1953. Episodes of diarrhea have occurred in association with two more attempts to attend college. The last failure occurred in December 1954 and he has had almost continuous symptoms since that time. After 234 days of hospitalization he is only now beginning to accept the realities of his disease and to show some signs of attaining some degree of emotional maturity. His colon was extensively involved at the time of the first examination and has changed little since then (Fig. 1).

Manifestations

Somewhat more than 65 per cent of the patients have exhibited a mild recurrent type of ulcerative colitis, characterized by mild to severe bloody diarrhea, associated with cramps, moderate fever, and colonic involvement varying from localized proctitis to disease of the entire colon and even including the terminal ileum. The individual episodes last from six weeks to three months, then subside to almost symptom-free intervals. Recurrences have been the rule, but complications have been infrequent. Some of these patients may develop intractable forms of the disease, particularly under severe continuing stressful situations.

This mild form of disease is illustrated by the record of a 30-year old coffee taster, who has been followed since 1948. He has been hospitalized five times with recurrences, and has had other milder attacks not requiring hospitalization. He has developed no complications and has been able to support a family during this time. There has been no apparent progression in the amount of colon involved in the eight years he has been under observation.

The second most frequent type of manifestation is the continuous intractable variety. About 33 per cent of the patients have fallen into this category. In this group, diarrhea, continuously or intermittently bloody, is the rule. The illness is prolonged and lasts longer than three months, usually 10-16 months or longer. Fever of moderate degree may be continuous or recurrent over long periods of time. Malnutrition with associated dehydration, vitamin and mineral deficiencies develop. The pulse rate is usually rapid and its rapidity is in excess of that to be expected from the fever present. This type manifestation may occur as the initial feature of the disease or it may be preceded by the mild episodic form. Extensive colonic involvement and involvement of the terminal

few inches of the colon have been common in this type. Complications are frequent. Therapy is particularly difficult, but patients with extensively damaged colons may sometimes undergo remarkable remissions of symptoms despite no apparent associated improvement in the appearance of the colon. The following case report illustrates the behavior of this intractable type of ulcerative colitis.

A young physician first had episodic attacks of the disease. At first only the rectum was involved, but the disease spread proximally so that eventually the entire colon and terminal few inches of the ileum were involved in the process. He developed continuous intractable symptoms which necessitated hospitalization for a total of 236 days and convalescence of something over a year. Despite extensive colonic injury he has made a remarkable recovery—and is able now to carry on a busy practice. His colon is unchanged as determined by barium enema examination. The sigmoidoscopic examination shows the mucosa to be edematous, friable and to have pseudopolypoid changes present. He usually has two or three stools a day, with some blood present occasionally, but he can carry on his daily activity in spite of these symptoms (Fig. 2).

Less than three per cent of patients with nonspecific ulcerative colitis have a fulminating type of disease, which is often fatal. This manifestation appears to be less frequent in New Orleans than is reported elsewhere. This fulminant form is characterized by excessive bloody diarrhea, excessive fever, excessive tachycardia, rapid development of severe electrolyte disturbances, and marked prostration. Death may occur from shock, perforation, hemorrhage or exhaustion. This variety may represent the initial manifestation of the disease or it may develop without apparent cause during the course of the other types.

As an illustration, the history of a 44-year old liquor salesman is typical. He developed a bloody diarrhea which within a week became very severe. The early course of his disease was characterized by hyperpyrexia, numerous gargantuan bloody bowel discharges, marked ileus, electrolyte disturbances and extreme prostration (Fig. 3). With intensive supportive therapy over a period of about 27 days he gradually improved and during the subsequent four months of hospitalization, the bowel symptoms became tolerably quiescent. In the ensuing seven years he has done remarkably well despite the fact that his colon has shown considerable progressive change (Fig. 4).

Complications

The development of complications and the relative frequency of the various types appears to be no different from those which are reported from other geographical locations. For convenience of discussion, I have divided these complications into those occurring primarily in the colon, systemic complications and, others not readily classifiable under these headings.

Colonic Complications:—Of the colonic complications pyogenic lesions about the anus, rectum and sigmoid were most common. These included ischiorectal abscess, fistula and pararectal or paracolic abscesses. One or more of these pyogenic processes occurred in 12 of 72 patients, or about 17 per cent. Pseudopolyposis of the colon was next most frequent and occurred in seven individuals or approximately 10 per cent of the subjects observed. Colonic stricture has occurred in three patients and in one of these, free perforation of the cecum complicated the resulting intestinal obstruction. Severe life-threatening hemorrhage occurred in another of the patients who developed a stricture. Carcinoma of the colon has not been observed in any of the patients

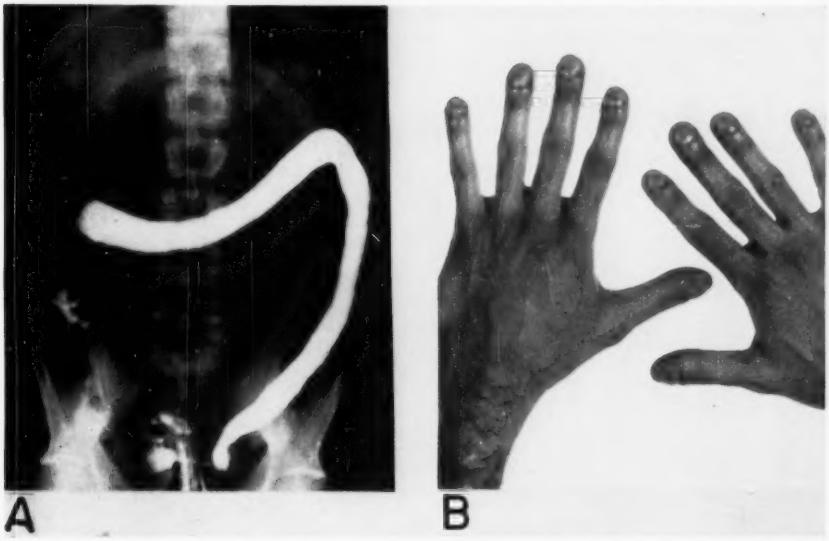

Fig. 1—A. X-ray film of colon of patient with severe intractable ulcerative colitis. This appearance noted at time of initial examination three years prior to time of the examination used for illustration. B. Clubbing of fingers in same patient.

whom I have seen. This, of course, should in no way be interpreted that cancer is less frequent in this locality.

Systemic Complications:—The most frequent accompaniment of the disease, particularly in the continuous intractable type is malnutrition of serious degree. This is characterized by weight loss, electrolyte disturbances, vitamin deficiencies, dehydration and general debility. Next most common was rheumatoid arthritis which occurred to a marked degree in five patients. *Pyodermia gangrenosum* was observed in four individuals. In one, considerable areas of denudition of the skin occurred. Of eight individuals whose livers were biopsied with the Vim-Silverman needle, four showed areas of focal necrosis, fibrosis and

fatty change. Ulceration in the mouth was present in six individuals. One of these exhibited severe recurrent aphthous ulceration, arthritis and *erythema multiforme*, which preceded the development of colonic manifestations by several months. Peptic ulcer has been observed to occur in three patients and in these, its occurrence was unrelated to steroid therapy.

Other complications include various types of abnormal immune responses. One patient has an acquired hemolytic mechanism which destroys red cells. He exhibits antiagglutination to a degree which makes crossmatching of blood extremely difficult. One patient has passed renal calculi repeatedly. Two other patients with concommitant idiopathic epilepsy have been seen, and a single instance of clubbing of the fingers and toes has been observed (Fig. 1).

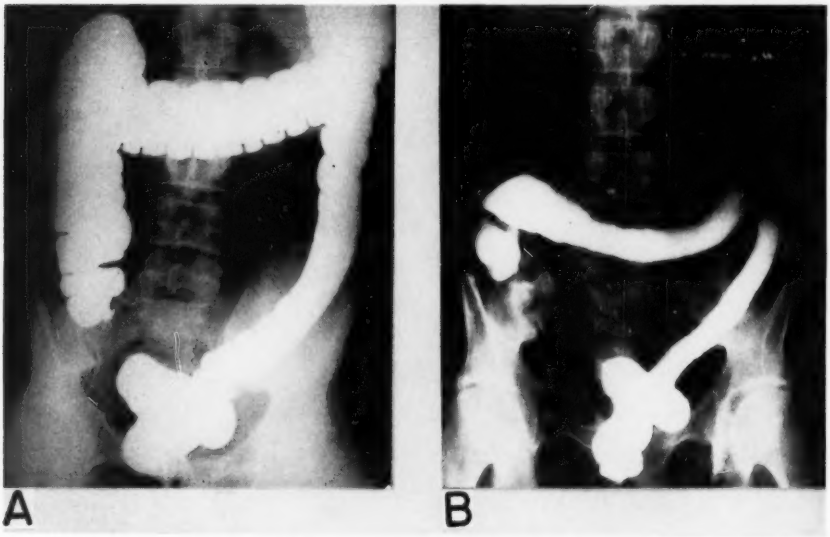

Fig. 2—X-ray examinations of colon of patient with intractable ulcerative colitis showing progressive involvement of colon. Even though colon at present appears even more markedly involved patient is able to carry on a vigorous medical practice.

Therapy

The medical management of patients with ulcerative colitis occurring in New Orleans is the same unsolved stimulating therapeutic problem which is present wherever the disease occurs.

These patients in general have received the wide variety of physical, and chemotherapeutic agents which have been used by other observers and the beneficial results obtained with these devices and agents with few exceptions is subject to considerable variation and interpretation. The mild intermittent type disease responds well to enthusiastically administered therapy of any

sort, including electroshock therapy. On the other hand, medical management of the severe intractable form of ulcerative colitis has all too often obtained disappointing results for the patient and a frustrating experience for the physician.

Antibiotics

Of the various agents used for therapy appropriate antibiotics have been extremely useful in the control of pyogenic complications and in preparation of patients for surgery. Convincing evidence that the use of these agents has modified the course of the disease in any other fashion is lacking in this series

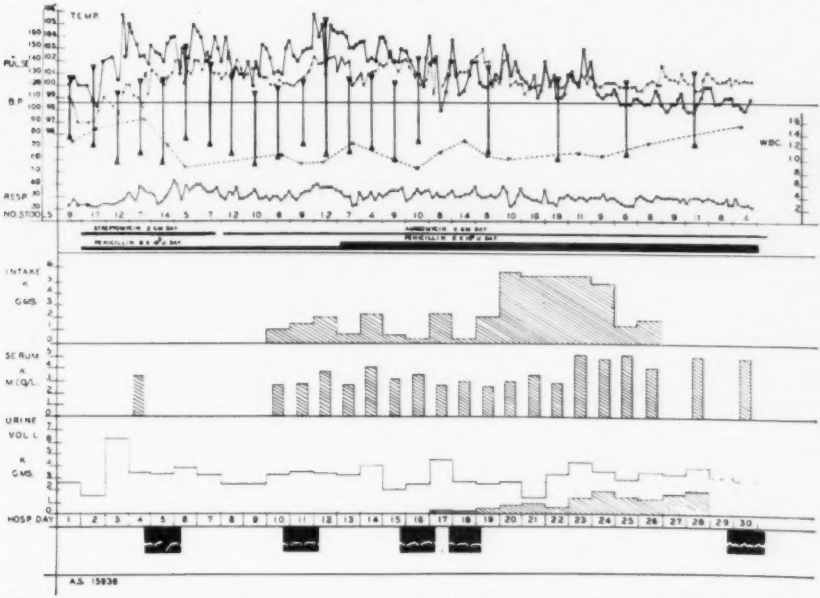

Fig. 3—Graphic representation of events occuring during an episode of fulminant ulcerative colitis. Note development of potassium deficiency and EKG changes.

of patients. Less useful were the sulfonamide compounds and various antilysozyme agents. Salicylazosulphapyridine (Azulfidine) has not proven to be as helpful with these patients as others have found it to be[13]. Nonspecific supportive therapy directed at the correction of nutritional deficiencies, replacement of blood and electrolytes has been an essential part of the treatment of this group of patients.

Corticotropin and Steroid Therapy

Twenty-three patients have been treated with either corticotropin, cortisone, or prednisone (Meticorten). Twenty patients either had remissions or

marked amelioration of symptoms. Eighteen have had recurrences after discontinuation of therapy. These results are not unlike those reported by Keifer

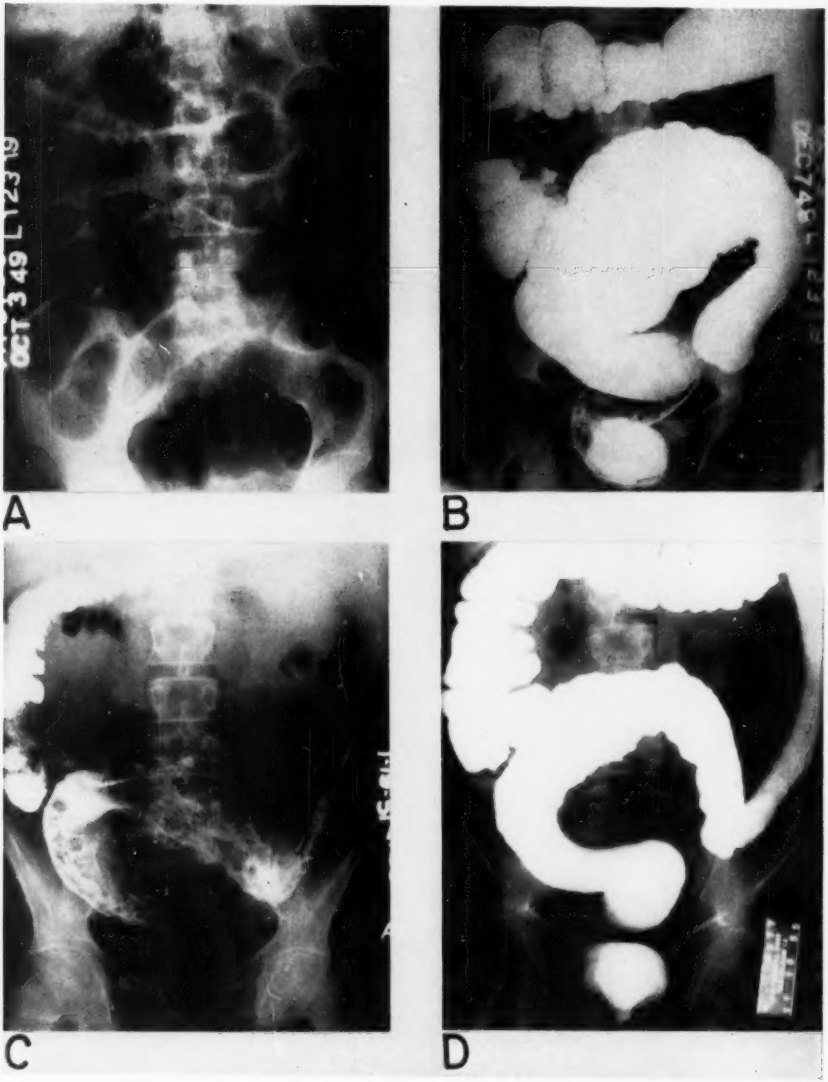

Fig. 4—Same patient as illustrated in Figure 3. A. Marked ileus at time of fulminant episode. B. Dilated loop of sigmoid about one month after fulminant episode subsided. C-D. Films illustrating progressive change in bowel in next six years.

and Elliott[14] and others[6]. There appeared to be little basis on which to make a choice of which of these agents to use except that oral steroid therapy is most convenient for prolonged administration. Prednisone therapy in three patients produced the desired effect without as much water retention. In the more acute cases intravenous ACTH was employed.

Two patients who have been treated with steroids and ACTH require special comment. One of these initiated his disease with continuous intractable symptoms. His entire colon and the terminal ileum rapidly became involved in the process. Severe crippling arthritis, nutritional failure, iritis, parotitis, *pyodemia gangrenosum*, pseudopolyposis of the colon, rectal stricture and a life-threatening hemorrhage complicated the basic disease process. He was placed on cortisone therapy in early 1950 with dramatic improvement. A colectomy was done in October 1950. After the colectomy the arthritis failed to subside and became a major issue in his rehabilitation and steroid therapy was reinstituted. He has remained on cortisone, 37.5–150 mg. a day, since that time. All attempts to discontinue the agent have been attended by a severe relapse of the arthritis. He has required three revisions of his ileostomy along with further resection of the terminal ileum because of recurrent hemorrhages. Periodically he has been hospitalized and ACTH therapy instituted. During this five-year period this patient has graduated from an engineering school with honors, fathered three children, earned a living as a teacher of electronics for the Air Force and in addition, operated a radio and television shop as a sideline.

The second of these patients had had ulcerative colitis for three years when first seen in 1949. At that time he was markedly emaciated, had severe symptoms of colitis, and was crippled with rheumatoid arthritis of the knees, ankles, hips, sacroiliac joints and spine. Locomotion was effected solely by means of a wheel chair. His mental outlook was one of despair and defeat. Cortisone therapy was started early in 1950, attended by a remarkable reversal of his colonic and mental symptoms. While on cortisone therapy he permitted orthopedic manipulation which fixed his joints so that he could be in an upright position and move about aided by crutches. He has subsequently married, and has one child. He has graduated from college and at the end of this year will get a Doctor of Philosophy degree in Psychology. All attempts at discontinuation of cortisone have caused a severe relapse of the colitis and reactivation of the arthritic process. His disease continues to smolder, however, and recently he has developed a fistula-in-ano.

Surgery

While medical management has sufficed for the care of most of these patients, eight, or 11 per cent have had colectomy and two more have had ileostomy alone. Two of the colectomies were done because of development of stricture, three because of severe pyogenic infections and the remainder, because of absolute failure of prolonged medical management. It is of interest

that colectomy in two patients with severe rheumatoid arthritis failed to alleviate this latter condition.

Psychotherapy

Psychotherapy is a fundamental part of the treatment of every patient with nonspecific ulcerative colitis. In personally managed patients it was always begun early, not as formal psychiatric treatment, but more as a sympathetic friendly discussion. While the technic varies from patient to patient, the bringing of warmth, a non-judging attitude and a sympathetic attention to complaints, has induced most patients to talk freely about their problems. Leading these individuals into concepts of maturity, reassuring them about their anxieties, teaching them devices by which their hostilities and aggressions may be discharged, have all proved rewarding. Particularly rewarding has been the direction of these aggressions into useful channels of accomplishment. When the problems of patients have been more deep-seated than this superficial type therapy is able to help, then more formal type treatment may be necessary. In these patients unwillingness to accept the need of psychotherapy has led to rejection of any help which they might obtain. With the approach which has been used in these patients, however, occasionally inner motivation may be developed so that psychiatric help will be acceptable.

Conclusion

It appears that nonspecific ulcerative colitis may occur less frequently in the New Orleans Area than in more northern latitudes. Except for the diminished frequency of the disease and the infrequent occurrence of the fulminant variety it in no way differs from that which occurs elsewhere.

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DOXINATE IN THE TREATMENT OF CONSTIPATION

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Recent work indicates that dioctyl sodium sulfosuccinate has proved useful in the treatment of certain types of constipation in infants and children[1,2], in immobilized patients[1] and in a variety of proctologic conditions[3]. A Council accepted brand name for dioctyl sodium sulfosuccinate is "Doxinate". This agent differs from all other substances previously used in the treatment of constipation since the action is solely that of fecal softening. Such an agent, if effective, would possess obvious advantages over traditional substances. Lack of bowel irritation would indirectly obviate the "habit forming" nature of the stimulant or irritant laxatives; lack of bulk would avoid the abnormal bowel distention caused by "bulk laxatives" as well as the danger of impaction inherent in these agents. Since dioctyl sodium sulfosuccinate is not an oil, no interference with the absorption of oil soluble vitamins would be expected as is the case with mineral oil. An additional advantage lies in the fact that very small doses are said to be effective.

Dioctyl sodium sulfosuccinate has been studied pharmacologically and the work has been reviewed[1]. It appears to be nontoxic and devoid of undesirable side-effects. Wilson and Dickinson administered as much as 50 mg./kg. to infants without noting ill effects.

The fecal softening action of dioctyl sodium sulfosuccinate depends upon reducing the surface tension at the oil-water interface in the heterogeneous fecal material. As a result, a softer and more homogeneous fecal mass is formed. Assuming that the average fecal elimination per 24 hour period is approximately 200 gm., a daily dose of 60 mg. to 120 mg. of dioctyl sodium sulfosuccinate would produce a concentration of about 0.03 to 0.06 per cent of the agent. This is adequate to reduce the surface tension at an experimental oil-water interface well below the 35 dyne/cm. figure at which "wetting" and consequent homogenization can be expected[4].

The N.N.R. monograph for dioctyl sodium sulfosuccinate points out the need for additional study of this agent in the common, less severe types of constipation. We have previously developed methods for the evaluation of various types of laxative agents[5] and because of our interest in the problem of

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proper bowel management we undertook to study the effectiveness of dioctyl sodium sulfosuccinate* for the treatment of several types of constipation.

Materials and Methods

One part of our study consisted of a comparison of the effect of dioctyl sodium sulfosuccinate with that of placebo therapy in patients with a long history of chronic functional constipation. For this study, 100 patients were chosen from the wards of the Chronic Disease Hospital, Long Island, Mass. All were

TABLE I

Results of Dioctyl Sodium Sulfosuccinate Therapy in Chronic Constipation

	Preliminary Observation	Placebo	Consecutive Treatment Periods	
			First Period (10 days)	Second Period (10 days)
Av. No. bowel movements per day	0.5	0.5	0.63	0.68
Av. consistency (1=watery; 5=extremely hard; 3=normal)	3.8	4.0	3.75	3.54
*No. times laxative or enema required	335	Not permitted	7	2
†No. times side-effects reported	196	230	139	57
Degree of patient satisfaction (3=good; 1=poor)	1.8	2.0	2.2	2.5

*Assuming one laxative or enema per day per patient, the maximum usage would total 740 (74 patients, 10 days). Of the 335 such measures used during preliminary observation, milk of magnesia was given 260 times, castor oil 60 times and enemas were used 15 times. During treatment, the 9 such instances were all enemas.
†Assuming all patients with all four recorded side-effects, the maximum would be 2960 (74 patients, 10 days, 4 side-effects).

immobilized or semi-ambulatory; all were permanently institutionalized; diet for all patients was identical throughout the study. The patients ranged in age from 35 to 93 years.

The technic of obtaining quantitative clinical data from subjective findings has been outlined[6] but the fundamental principles bear repetition. Briefly they

*Dioctyl sodium sulfosuccinate was supplied as Doxinate by Lloyd Bros., Inc., Cincinnati, Ohio, in the form of 20 mg. and 60 mg. soft gelatin capsules. Doxinate is a Council accepted brand of this chemical.

are randomized sequence of administration and "double blind" conditions. The medicament and placebo, method of coding and choice of placebo or control should be carried out so as to insure that neither observer nor subject can identify the medication. This technic permits subjective observations to be converted to an impartial quantitative basis if numerical values are assigned to the variations in each kind of observation. These experimental conditions were established in the present study. The principle of clinical trial as the final court of appeal in the test of the efficacy of a medicament has been commented on editorially[7]. Previous studies by us[8] have shown the fallacy of failure to properly quantitate and analyze subjective results.

In this study we recorded the average number of bowel movements per day, the consistency of the stool, required frequency of laxation or enema, the degree of patient satisfaction and side-effects present. Stool consistency was rated on a scale of 1 = watery; 3 = soft, formed normal stool; 5 = extremely hard. Degree of patient satisfaction was recorded once daily and expressed as 1—poor, 2—fair, 3—good. Side-effects were elicited by daily questioning.

All of the 100 patients were observed for a 10-day period and records made as described above. Half the group then received dioctyl sodium sulfosuccinate, 60 mg. daily, for a period of 20 days followed by placebo for a period of 10 days. The other half received the placebo for 10 days followed by dioctyl sodium sulfosuccinate for 20 days. Both medication and placebo were supplied as small soft gelatin capsules identical in size, shape and color. Placebo and medicament were coded and neither the patient nor the attendants knew which was being administered.

Enemas and laxatives were permitted as necessary or as desired throughout the study except that none were permitted during the period of placebo therapy unless urgently necessary. Only one such occurrence was noted. In the majority of cases, stool consistency was verified by an attending nurse. Subjective data was obtained by careful, experienced questioning. A total of 74 patients completed the study.

Clinical observations were made on an additional 40 patients who received dioctyl sodium sulfosuccinate for constipation due to or accompanying a number of diverse conditions. Redundant bowel, Hirschsprung's disease, multiple sclerosis, cerebral accident, cardiac conditions, the presence of hemorrhoids, the use of narcotics or the prolonged use of psychodynamic drugs such as chlorpromazine was present in this group. Several were postoperative cases. Dosage varied from 60 mg. once daily to 180 mg. of dioctyl sodium sulfosuccinate per day. This group represents a series of special surgical and hospital problems which were treated with dioctyl sodium sulfosuccinate to enlarge the scope of the evaluation and to form an impression of its value in specific conditions wherein the application of the "double blind" technic was not practical.

Results

Chronic functional constipation:—Results in the 74 patients with chronic constipation are shown in Table I. In order to better assess the value of continuing medication, results for each of the two consecutive 10-day medication periods are listed separately.

Certain conclusions can readily be drawn from the data shown. The average number of bowel movements during the treatment period is significantly higher than during the placebo period. The figures correspond to improvement from one movement every two days to two movements in each three day span. Furthermore, the frequency increases with continued treatment. Although these data are convincing, they become dramatic indeed when it is noted that the increase occurred at the same time that the need for enemas and laxatives fell

TABLE II

Side-Effects Present in Constipation, During Catharsis and During Dioctyl Sodium Sulfosuccinate Therapy

Patient Complaint	Placebo Therapy	Catharsis	Consecutive Treatment Periods	
			First Period (10 days)	Second Period (10 days)
Gas	85	60	55	16
Cramps	83	99	58	32
Fullness	47	36	22	8
Nausea	15	1	4	1
Total	230	196	139	57

to a negligible figure. Thus, in the second treatment period, our patients averaged 0.68 bowel movements per day of nearly normal consistency and required only 2 enemas and no laxatives as compared to 335 enemas or laxatives during the observation period.

Side-effects noted were greatly decreased. The values of 196 and 230 seen during observation and placebo administration were probably due to discomfort from laxation and from constipation, respectively in the two groups. During the first 10 days medication with dioctyl sodium sulfosuccinate, the number of such effects fell to 139. The further drop to only 57 such recorded instances among 74 patients over the second 10-day period is convincing evidence both of the freedom from side-effects of dioctyl sodium sulfosuccinate and the relief of discomfort which it provided. The nature and frequency of these patient complaints is shown in Table II.

Patient satisfaction cannot be discounted as an important factor in the selection of proper anticonstipation therapy. This intangible psychologic factor has an important part in determining the patient's cooperation with the prescribed therapeutic regimen and his willingness to accept treatment. Our data show that the patients in our series were fairly well pleased with either placebo treatment (index 2.05) or enema and laxation (index 1.83). During treatment the index rose to 2.2 (better than fair) during the first 10-day treatment period and finally approached the "good" index of 3.0 during the second 10 days of treatment.

An additional point of interest is apparent from the data. During placebo administration, side-effects increased over those present during traditional laxation methods. Cramping decreased, while the symptoms referable to the filled bowel increased as would be expected. We regard this both as evidence of the reliability of our technic and as an indication of the primary cause of the patient's dependence on laxatives. In earlier studies[4] we noted that "The inadequate number of bowel movements and the accompanying side-effects in the period of placebo medication negates the frequent supposition that laxatives are unnecessary in such a population of chronically constipated patients."

In our series of 40 additional clinical cases we found dioctyl sodium sulfosuccinate to be of real value as a fecal softener provided enemas or proper laxation was used adjunctively to aid elimination. In the majority of these conditions, loss of tonus or suppression of the anal reflex makes frequent laxation necessary to avoid impaction. Even then the stool is hard; griping and tenesmus are common. The routine continuing administration of dioctyl sodium sulfosuccinate was found to maintain the feces in a soft normal form so that laxation could be decreased to 4 or 5 day intervals without tenesmus at passage and with no danger of impaction.

Several case summaries from the group are of interest. Patient M.L., a 54-year old female psychiatric patient, was severely constipated, presumably as a side-effect of chlorpromazine. She had undergone surgery 7 times including cholecystectomy and removal of a polyp from the colon. X-ray studies showed partial obstruction of the large bowel with atonicity and "ballooning" of the area behind the obstruction. Saline cathartics had been tried but invariably produced very severe cramping; enemas were ineffective because of the difficulty in reaching the area involved. Daily administration of 180 mg. dioctyl sodium sulfosuccinate with saline cathartic every 5th day has resulted in soft stools with no cramping or other side-effects.

Patient G.D., a 46-year old male psychiatric patient required psychodynamic treatment with chlorpromazine. Complete obstipation resulted. A thorough enema followed by dioctyl sodium sulfosuccinate, 180 mg. daily, has resulted in complete correction of the constipation despite continued chlorpromazine therapy.

Patient C.G., a 68-year old male had a long history of constipation. Barium meal studies showed a large redundant descending colon with an estimated 2 foot loop of redundant bowel. Fecal material presumably fills the loop and hardens, so that laxation is quite unsatisfactory. On the other hand, with dioctyl sodium sulfosuccinate bowel movement has returned to a relatively normal status. It appears that if the fecal material in the redundant loop can be kept soft, peristalsis can move the mass satisfactorily. An x-ray of this interesting case is included.

Comment

The voluminous medical literature dealing with constipation and its treatment is the best evidence of the importance and frequency of this therapeutic problem. Every physician meets the problem many times over in his daily practice.

Modern therapy in constipation is based on the sound physiologic principles of proper diet, water intake, habit time, etc. The purgative or laxative "insult to the bowel" is largely discredited and therapeutic agents are sought which aid in restoring normal physiology. The supposition that constipation requires no therapy is unsound since the side-effects seen in constipated patients make treatment most desirable[6].

In previous publications we have studied the effectiveness of psyllium seed, mineral oil, cascara sagrada, milk of magnesia, and methyl cellulose[8]. Each of these agents offers advantages and disadvantages. Thus, the irritant or stimulant agents tend to empty the bowel and create the conditions leading to a subsequent episode of constipation. Mineral oil, although often effective, may cause excessive flatulence, unpleasant "leakage" and may interfere with vitamin absorption. The psyllium "bulk laxatives" offer important advantages[5] but excessive doses are often required and there is danger of impaction if water intake is inadequate.

We have found dioctyl sodium sulfosuccinate to be a useful agent in the treatment of several types of constipation. This new fecal softener appears to be without "laxative" action. Where abnormally hard feces, therefore, is the predominant factor in the constipated patient, dioctyl sodium sulfosuccinate results in restoration of normal function both in terms of stool consistency and frequency. In the less common cases where inadequate peristalsis is a primary factor, additional laxation may be necessary. Even here, however, dioctyl sodium sulfosuccinate tends to maintain a soft fecal mass which makes the required laxation less frequent and more effective.

Results in our series of cases with relatively severe chronic functional constipation were dramatic. Not only did stool consistency approach the normal

with dioctyl sodium sulfosuccinate, but frequency improved and the use of enemas and laxatives was diminished. This agent, therefore, was not only of real benefit to the patient but it provided an important economic saving for the hospital.

Summary

We have studied the action of dioctyl sodium sulfosuccinate, a fecal softener, in a series of patients with chronic functional constipation. The validity of the technics used has previouly been established. The use of this agent resulted in easier passage of the softened stools, increased frequency of bowel movements and increased patient satisfaction. Side-effects of both laxation and constipation itself were markedly reduced. The need for enemas and laxatives became negligible. Administration over a period of 20 days or more is desirable.

Dioctyl sodium sulfosuccinate appears to be an efficient fecal softener which combines the desirable effects of bulk laxatives with a lubricating action. It represents, therefore, a definite advance in the management of the bowel problem. No evidences of toxicity were seen.

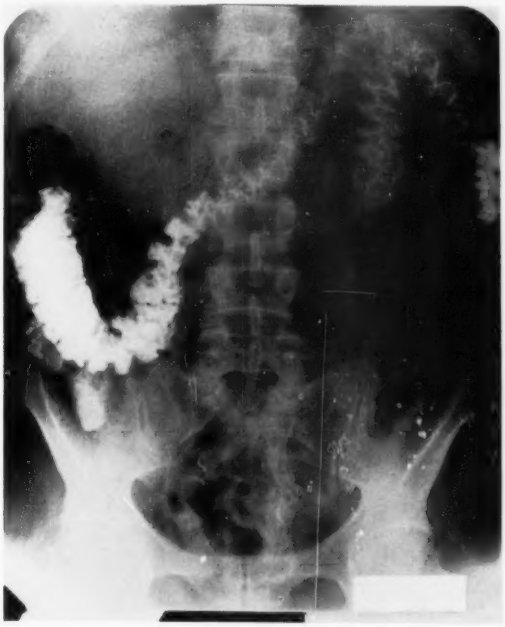

Fig. 1—X-ray showing redundant loop in patient C.G.

In severe constipation due to disease or depressant drug action, fecal softening alone may not always be adequate. Routine use of dioctyl sodium sulfosuccinate, however, is advantageous in reducing the required frequency of laxation and in promoting easier passage of a softer stool.

One of the outstanding advantages of the use of dioctyl sodium sulfosuccinate is that the full daily dosage of one or two small capsules can be given at one time with no necessity for administration several times a day. This is an important factor in patient acceptance and in hospital convenience.

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HETEROTOPIC PANCREATIC TISSUE IN THE STOMACH*

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Heterotopic pancreatic tissue is not rare and, since Schultz[18] first described it in 1727 and Klob[12] reported his histologic studies in 1859, it has been found in almost every tissue in the body. Various studies[2,3,5,6] have reported the incidence of this tissue as 0.6 to 5.6 per cent of autopsied cases. Waugh and Harding[21], in reviewing the autopsy findings of Leuble, Opie and Katsuroda, Feyster and Duff, Foster and Bryon, found the incidence to be about 1 per cent of tumors of the stomach.

The most common locations for heterotopic pancreatic tissue are the stomach, duodenum, jejunum and Meckel's diverticulum, about 27 per cent occurring in the stomach. In a review of the literature, Palmer[15] found 215 cases of histologically proved aberrant pancreatic tumors in the stomach.

Several theories have been offered as to the origin of heterotopic pancreatic tissue. King and MacCallum[11] believed the condition to be acquired and secondary to chronic inflammation. This theory has been fairly well disproved by Benner[3] and others. Most authors maintain that this anomaly is antenatal in origin.

Benner[3] suggested two possible etiologies of heterotopic gastric pancreas, or so-called pseudodiverticulum. He said "it may be the primary anomaly, which, if occurring early in development, the pluripotentiality of the gut epithelium would allow to differentiate into pancreatic-like structures." The occasional presence of pancreatic scini within the *lamina propria* would suggest a local origin from gut epithelium. The apparent opening of some of the ducts into pseudodiverticula is consistent with the theory of a local origin, and the inward protrusion of the crater is supportive evidence for a primary rather than a secondary alteration. The development of the diverticula, however, may be secondary to the presence of the pancreatic tissue. Bologenesi[4] was able to produce diverticula in the duodenums of dogs by the implantation of pancreatic tissue.

Warthin's concept[19] that "accessory pancreatic tissue is formed from lateral budding of the rudimentary pancreatic ducts as they penetrate the intestinal

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wall, the mass of pancreatic tissue thus formed being snared off and carried by the longitudinal growth of the intestine upward and downward" does not stand up, as pointed out by Pearson[16], in those instances in which the pancreatic nodule is outside the gastrointestinal tract.

In lower forms of animal life and fishes the pancreas is not a localized organ but is distributed along the gastrointestinal tract. A reversion of the pan-

Fig. 1—A characteristic x-ray of aberrant pancreatic tissue in the stomach wall. A filling-defect is present with a fleck of barium in the center representing the dimple in the crater.

creatic tissue to a more primitive type may explain its wide distribution along the gastrointestinal tract.

The pancreatic masses may be loosely adherent to the serosal surface of the intestine or may appear in the subserosa, submuscularis or submucosa. Benner[3] gave an excellent description of the anatomy of gastric heterotopic

pancreas, which, he said, was an elevated mound with a central dimpling and an opening forming a pseudodiverticulum. Waugh and Harding[21], Branch and Gross[5], Chapman[7], Faust and Mudgett[8], Barbosa[2], Busard and Walters[6], Roach and Poppel[17], have all described cases with similar findings. Benner[3] also mentioned the filling of the dimpling of the heterotopic pancreas with barium so that it resembled a polyp with an ulcer at its tip.

Gastric pancreatic tissue causes symptoms in approximately 50 per cent of cases. There may be various gastrointestinal disturbances as well as evidence of biliary obstruction. Palmer[15] found the presenting symptom to be epigastric pain in three-quarters of his patients, and pyloric obstruction was present in 25 per cent of adults having this anomaly. Other symptoms are reported as hemorrhage, chest pain, anorexia, weight loss, nausea and vomiting.

Although Leodolter[13] suggested that the diagnosis of heterotopic pancreatic tissue of the stomach was possible by x-ray examination, a review of the literature does not reveal a single case diagnosed either clinically or by x-ray examination prior to operation. Palmer[15] stated "it is necessary to admit, with du Bourguet and Berge, that probably neither a clinical nor x-ray diagnosis has ever been made exactly."

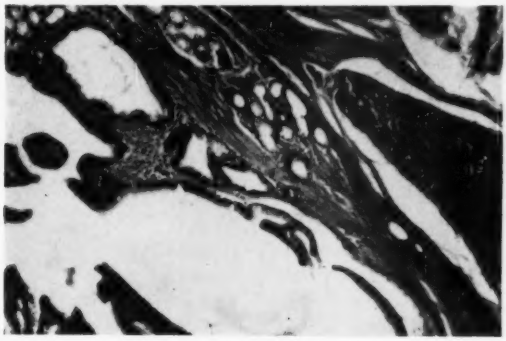

Fig. 2—Section showing aberrant pancreatic tissue in stomach wall. Hematoxylin and eosin approximately x 50.

Radiologically, most pancreatic rests produce a nodular prominence in the gastric mucosa with a corresponding indentation and filling defect in the barium shadow. The mass seldom exceeds 4 cm. in diameter and is usually found in the antrum. A central depression should be sought but may be overlooked because of its small size or because it is obscured by tenacious mucus. A definite diagnosis can be made only by excision biopsy.

The treatment of either symptomatic or incidentally discovered pancreatic heterotopia is surgical excision. A frozen section should be made at the time of

operation. Many of these tumors in the stomach are located in the pyloric region and narrowing of the pylorus may occur after resection so that pyloroplasty may be indicated.

Case Reports

Two cases of heterotopic pancreatic tissue of the stomach are reported in this paper. Both fit Benner's description, including the x-ray appearance after

Fig. 3—X-ray of Case 2 showing the characteristic picture of aberrant pancreatic tissue in the gastric wall.

barium. After seeing our first case, the second was immediately recognized at operation by its characteristic appearance.

Case 1:—R.L. A 60-year old white female was admitted to the hospital with a long history of nervousness and multiple complaints. A routine examination

prior to admission had included a gastrointestinal barium study which had revealed a rounded translucent defect in the prepyloric segment of the stomach on the anterior wall near the greater curvature which resembled a polyp (Fig. 1). A hiatal hernia was also demonstrated. Gastroscopic examination failed to visualize the lesion well.

An exploratory operation was performed and, on gastrotomy, an 0.8 cm. intramural mass was found on the anterior wall near the greater curvature approximately 2 cm. proximal to the pylorus. It was elevated, with dimple in the center, resembling a diverticulum. When frozen section showed the lesion to be benign, local resection of the mass was performed and the hiatal hernia was repaired from below. The patient had an uneventful recovery.

The specimen measured 3 x 3 cm. and one surface was covered by mucosa (Fig. 2). In the center was an elevated nipple-like mass, with a dimple in its

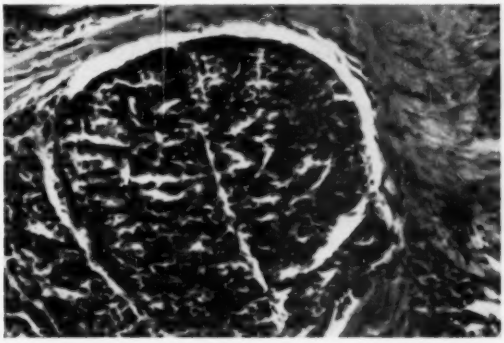

Fig. 4—High power view of pancreatic tissue surrounded by gastric musculature. Hematoxylin and eosin approximately x 300.

center, resembling a diverticulum. The pathologist's final report was a polypoid gastric mass containing ectopic pancreatic tissue.

Case 2:—J.M. A 50-year old white male was admitted to the hospital after a general check-up, in the course of which a gastrointestinal series had revealed a gastric lesion. The patient was entirely asymptomatic except for chest pain. The radiologist had described the lesion (Fig. 3) as follows: "There is present, in the immediate prepyloric region on the greater curvature side, a sharply defined circular filling defect measuring 1.1 cm. in diameter. Within this defect is a centrally situated diamond-shaped fleck which is constant in appearance. The size and position of the defect and the central fleck, which suggests umbilication, presumably are characteristic of an aberrant pancreatic nodule, although it is conceivable that an ulcerated tumor arising in the deeper layers of the

stomach might produce a similar appearance. No other organic lesion of the stomach is seen."

At exploratory laparotomy a mass was felt in the region of the pylorus on the anterior wall of the stomach. A gastrotomy was performed and an elevated mass was found with a dimpling in the center. This was widely removed and identified in frozen section by the pathologist as pancreatic tissue. The gastrotomy was closed and the patient had an uneventful recovery.

The pathologist's final report was "The specimen measured 2.5 x 3 cm. and was covered by mucosa. There appears to be a diverticulum in the mucosal surface (Fig. 4). Sections show the gastric mucosa to have an umbilicated appearance and to have this channel partially lined by pancreatic epithelium. The ectopic tissue also extends into the gastric wall involving the serosa."

Conclusion

Two cases have been presented to point out that the diagnosis of heterotopic pancreas of the stomach can be made in many cases by x-ray examination if the condition is kept in mind. The lesion is not rare, as evidenced by the increasing number of cases reported in literature in the past few years.

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OPERATIVE CHOLANGIOGRAPHY*

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Excepting in unusual circumstances, investigation and evaluation of the bile ducts should be a part of every cholecystectomy. There have been established certain well accepted indications for exploring the common duct[6]. These may be listed as:

1. Palpable stones in the common duct.
2. History of jaundice associated with colicky pain and perhaps fever.
3. Dilated and/or thickened common duct.
4. Dilated cystic duct.
5. Enlarged head of the pancreas.

There are, however, definite limitations and defects in common duct exploration, and it is therefore a procedure not to be used needlessly and not without full knowledge of its limitations. There is a definitely higher morbidity and mortality in cases subjected to choledochostomy[6]. It is questionable that the mortality increase is entirely chargeable to the procedure itself, yet it is generally conceded that it is fraught with added risks. Mixter et al[20] have pointed out, moreover, that even using well established criteria, there have been 50 per cent negative common duct explorations. McKittrick and Wilson[17] explored 100 per cent of a series of cases with 50 per cent negative results. The percentage of negative exploration even by the best surgeons varies from 3.9 to 71.1 per cent [15,18,24]. Furthermore, even in the best of hands, common duct stones have been left behind after common duct exploration. Lahey[16] reported that at least 10 per cent of patients had stones left in the common or hepatic ducts following surgery. Mixter[19] reported that 20 per cent of a group of 41 who had an exploration of the common duct for stones had residual stones shown on delayed cholangiography. Hepatic stones are difficult to detect by exploring the ducts. Similarly, ductal anomalies are not detectable prior to dissection, which may damage the common duct, and some strictures or narrowing of the ampulla of Vater may be undetected by probing.

Here then is a procedure of common duct exploration in which: 1. even using accepted criteria, in many cases the procedure proves to have been unnecessary, 2. even in excellent hands stones have been overlooked, and 3. the procedure adds appreciably to the morbidity and to some degree to the mor-

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tality. The need for other procedures in evaluation of the ductal system is apparent.

Delayed cholangiography through the T-tube, subsequent to surgery and prior to removal of the T-tube seems to be well accepted. It seems to be obvious that if the procedure is able to give information as to retained stones or patency of the bile ducts, it would be better to have that information at the time of the original surgery. It is available by use of operative cholangiography and it is a little surprising, perhaps, at the reluctance of many excellent surgeons to use it despite the dangers and defects of depending only on common duct exploration. Add to this the fact that hepatic stone visualization and anatomical stricture or anomalies of the biliary duct are only properly studied by cholangiography and one wonders at the lack of general use of the procedure.

There are, of course, reasons for this attitude of nonacceptance of the procedure of operative cholangiography. As Sherman and Stabins[23] point out, it is possibly due to lack of experience in the procedure and in the initial difficulties in interpretation and joint preparations between surgery, anesthesia and radiology. There are certain well-known causes for difficulties in operative cholangiography, such as incomplete filling, spillage, motion, poor timing, air bubbles, interpretation. As one gains experience, the percentage of errors steadily decreases. Hicken[8] has reported his percentage of error as 2 per cent and decreasing.

There are certain questions about operative cholangiography that must be answered. First, how reliable and valuable is the procedure and is it possible to be more accurate using it than by opening the common duct? As noted above, the more one uses the procedure, the less are the technical errors and errors in interpretation, which are not properly chargeable to the procedure itself. Mixter[19] reporting on 72 patients who had normal cholangiograms at the end of surgery found that none needed re-exploration, indicating a high degree of accuracy. Contrasted with this, in 41 patients without the benefit of operative cholangiography, 11 showed stones on delayed cholangiography, 4 requiring re-operation. Brown and Brown[3] found, in 150 cases, 98 per cent correlation between x-ray findings and findings on exploration of the common duct. Mixter et al[20] reported on 147 cases in which, based on findings of operative cholangiography, the common duct was not explored. Without the cholangiogram, 107 of these would have required common duct exploration, based on usual criteria; the other 40 would not have been explored anyhow. In following 131 of these 147, in only 6 (4.5 per cent) did symptoms persist, suggesting possible failure of operative cholangiography to reveal retained stones. Hicken[8] states that 20 per cent of all common duct stones removed could not be palpated but all were detected by operative cholangiography. Hepatic stones occur in 6-7 per cent of all cases and their detection depends almost entirely on cholangiography. Hicken[8] states that in 18 per cent of patients there occur biliary tract anomalies

best detectable by this procedure. Douglas[5] in 108 cases in which cholangiography was done found stones overlooked in 3 cases—in one the technic was definitely in error, so that was 2 failures in 108 cases, considerably less than failures by opening the common duct.

In 20-25 per cent of cases, operative cholangiography obviates the necessity of opening the common duct in the face of findings which otherwise would require such an exploration[20]. Six to seven per cent of cases have hepatic duct stones which are difficult to detect by ordinary exploration.

It may be categorically stated that the procedure causes no morbidity or mortality. A few cases of fever and discomfort, presumably due to cholangitis, occur, but these rapidly subside and do not prolong hospitalization.

It appears, therefore, that the procedure, once perfected, has a high degree of dependability and will obviate opening the common duct in an appreciable number that otherwise would require exploration. Common ducts must still be explored if there is any question about the cholangiogram but certainly less will require it using this procedure primarily.

Numerous technics have been used in doing cholangiography. Without going into details, the use of 35 per cent diodrast seems to be preferable. The dye may be injected through the gallbladder, cystic duct or into the common duct using a needle, or catheter. Personally, we prefer, whenever possible, to cannulate the cystic duct, using a specially prepared catheter[1]. If this is not possible, then injection with an angulated needle is made directly into the common duct.

Conclusions

1. *Operative Cholangiography* in a valuable method in biliary tract surgery.
2. It supplements—not replaces—other procedures.
3. Its use reduces number of common duct explorations.
4. It is a reliable method once its use is perfected.
5. It gives valuable information about ductal stones, strictures, anomalies and ampullary lesions.

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OPERATIVE USE OF FIBRIN CLOT CHOLEDOCHOLITHOTOMY

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Introduction

Some day there will be no residual stones after surgical exploration of the biliary ducts. Until then, two groups of operative procedures are useful.

One is anastomosis of the common duct to the duodenum (or intestine) as advocated by Walters[1] and Stock[2]. The second, is to provide a wide lumen through the termination for the bile duct by transcholedochal dilatation[3] or by transduodenal sphincterotomy[4].

These procedures may also have undesirable sequellae[5]. For example, ascending cholangitis may follow duct-duodenal anastomosis. Sphincterotomy, on the other hand, may be complicated by stricture.

I have investigated a new procedure to solve this problem. It involves the formation of a fibrin clot within the bile duct[6] so that debris or calculi would be enmeshed in the coagulum (Fig. 1).

Dees[7] used bovine fibrinogen for renal calculi. He has reported that in a good firm clot, tensile strength ranges from 125 to 160 gm. He has further found that the average coagulum has tensile strength from 40 to 65 gm. with a stretch of the coagulum of 25 to 30 per cent before the clot breaks.

Procedure

For use in the patient, solutions are prepared preoperatively. Human fibrinogen (Parenogen-Cutter) is prepared with accompanying diluent (to contain 20 mg. per c.c.). Thrombin (Parke, Davis & Co.) is prepared with water (50 NIH units per c.c.).

The duct is explored. Calculi are removed. The duct is washed with saline; its capacity and emptying rate are determined. The T-drain is placed and sutures inserted[8]. The duct is irrigated with water. Fibrinogen is instilled (200 per cent of duct volume). Thrombin solution is then added (50 per cent of duct volume). Twelve minutes elapse during which the gallbladder may be removed.

Fibrin clot is withdrawn with assistance of (Babcock, ring, smooth or rat tooth) forceps as the T-drain is removed. (The neurological suction tip has been used to remove the clot). The duct is then irrigated. Any syringe may be used. Urethral or ureteral catheters will facilitate the lavage.

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After irrigation of the ducts, an operative cholangiogram is done. For best interpretation, a scout film, and two exposures after injection of the radioopaque media are taken.

Comment

The fibrin clot maneuver has been used in nine patients to date. Eight patients are well from three to twelve months. One patient of 78 years had cardiac arrest massaged for 45 minutes at the conclusion of operation. He recovered and was talking to his family 36 hours later when he suddenly died. Clot was poor in two of the nine patients and the procedure was not efficient.

There are several factors to assess.

First, in two of these nine patients, a poor clot was formed. This was due to deviations from exactly neutral pH. For example, reconstituted fibrinogen has

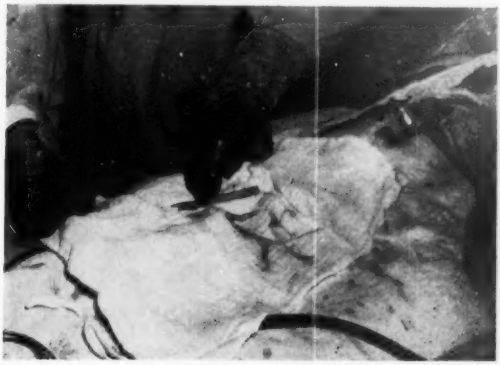

Fig. 1—Fibrin clot removed with T-drain from biliary tract at operation for choledecholithiasis.

a pH of 5.8-6.2. This is neutralized before use by N/10 NaOH to pH of 7.0 as indicated by bromthymol blue. From 5 to 10 c.c. of the base is needed for the 50 c.c vial of Parenogen.

On the other hand excessive alkalinity due to hepatic bile will also interfere with clot formation. Normally the pH of hepatic bile is from 7.1[9] to 8.6[10]. This is overcome by sufficient preliminary irrigation of the ducts.

A second factor is that of cholangitis. Obviously aseptic precautions are observed. Particular attention is given to the sodium hydroxide solution.

A third consideration is possible transmissibility of hepatitis. It has not been observed in these patients.

A fourth factor is the possibility of duct obstruction due to residual fibrin clot. Because of the lytic effect of the bile this possibility is decreased. Postoperatively the duct system is irrigated daily (or oftener) with saline. In addition, if the bile flow is not adequate, Varidase (Streptokinase) is instilled. The lytic effect of bile has not been a deterrent to clot formation; it actually expedites removal of the clot from the smaller intrahepatic radicles.

The recognition of intraductal calculi at operation may be difficult. Even so, it may be possible to use a relatively harmless procedure to assure that calculi, identified or not, could be removed. The use of the fibrin clot, however, will not enmesh calculi larger than one cm. in diameter, or those which may be imbedded in choledochal diverticula.

Summary

A method is reported for operative removal of small biliary calculi by use of fibrin clot.

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AMEBIASIS TREATED WITH BIALLYLAMICOL HYDROCHLORIDE

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While human amebiasis has been generally recognized with increasing frequency there has not yet been available a single therapeutic agent which satisfactorily treated all manifestations of the disease with a high rate of cure. The present report summarizes a study which began in January, 1955 using a new medication, Biallylamicol hydrochloride, in 25 patients with various disturbances from human amebiasis.

The incidence of intestinal amebiasis undoubtedly has great geographical variability depending on climate, water supply, sewage disposal, population concentration and many other natural and sanitary factors. In any effort to report the percentage incidence in any area, all of these factors as well as the clinical thoroughness and laboratory skill in effecting a diagnosis offer innumerable variables.

The patients in this study were derived from private practice and all lived in the environs of Jackson, Mich. The city has an excellent water supply but the sewage system, as in many growing communities, has become overloaded. With heavy rains many basements are flooded due to backing up through the sewers of the run-off since no separate storm sewers exist. Perhaps the fact that a definite percentage of the population lives just outside the city in low-lying suburban communities, serviced by wells and cesspools, also contributes to intestinal disease. One of the patients was a retired missionary who lived in India for many years and had recurring dysentery ever since her first stay in India.

No attempt to derive a figure for the incidence of amebiasis in this community was made in the present study because the patients were selectively and not routinely investigated. It can probably be assumed, however, that the incidence in southern Michigan should approximate that of neighboring Ohio. In 1953 McHardy[1] reported an incidence of 2 per cent and the same figure was more recently given for Ohio by other investigators[2] making a routine stool analysis on every patient examined.

The final diagnosis in the present group of patients was based on the immediate examination of freshly passed stools obtained following saline purgation. The routine procedure in all patients was for the patient to report to the laboratory at 8 A.M. by appointment. A light breakfast prior to reporting was permitted. They were then usually given two ounces of Fleets phospho-soda. Occasionally another saline cathartic was given in comparable dosage and in some patients the dosage was decreased depending upon symptoms. Thereafter the patients handed the freshly passed stool specimens directly to the laboratory

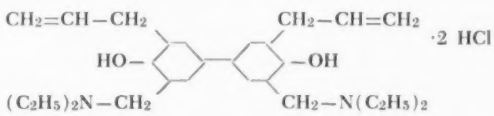
technologists who made an immediate warm stage microscopic examination. Three successive stool specimens were examined at each appointment except in those rare instances when only two specimens were obtained. Working by appointment made it possible for the technicians to devote sufficient time to the tedious and distasteful job of making an adequate study of each specimen. Despite these careful examinations false negatives undoubtedly occur and serve to emphasize the many problems in clinical and laboratory diagnosis. Such problems have been most comprehensively reviewed in the excellent monograph by Rees[3]. Except for identification of the *Endameba histolytica* no other definite diagnostic test exists.

In the accompanying table it should be noted that in 15 of the patients active motile trophozoites of *Endameba histolytica* were found and in all of the remaining patients the diagnosis was based on the presence of precysts and cystic forms of *Endameba histolytica*. No patient who did not have positive stool identification was included in the present study. Those patients who had prior therapy for amebiasis were treatment failures of other medications and none had been previously treated with Biallylamicol. All patients had symptomatic dysentery. A majority of the patients had proctoscopic and sigmoidoscopic examinations.

Biallylamicol hydrochloride is a relatively new amebacide which was synthesized in the Parke-Davis Research Laboratories[4]. It has recently been made generally available by Parke, Davis and Company under the trade name of "Camoform" and supplied in 250 mg. tablets. It has also been referred to by earlier investigators as PAA-701[5,6] and SN 6771[7].

Biallylamicol is a synthetic organic chemical containing neither iodine nor arsenic in its molecule. Experimental work with animal amebiasis indicated definite therapeutic effectiveness[8]. While the effects of Biallylamicol were diminished by gastric mucin they were not abolished. Experiments with egg-yolk infusions with 4.3 per cent gastric mucin demonstrated amebacidal activity in 1:5000 and amebistatic activity at 1:15000 dilutions[9].

Chemically the drug is a white crystalline substance readily soluble in water. The drug is identified chemically as:



6,6′-diallyl-α, α'-bis (diethylamino)-4,4′-bi-o-cresol, dihydrochloride.

Data on physiological distribution[9] show that during daily administrations from 70 to 80 per cent of the daily oral dose was absorbed from the gastro-

intestinal tract; less than 0.5 per cent of the dose was excreted in the urine. With cessation of administration, plasma levels dropped 60 per cent in the first three days but at the end of three weeks 15 per cent was still present. The drug may be found in the urine for as long as six weeks. This evidence suggests considerable tissue localization of Biallylamicol. Thompson, et al[8], in addition to the lack of drug toxicity and rapid gastrointestinal absorption quoted the following additional features[10] indicating consideration of the drug to be worthwhile in antiamebic therapy: high concentrations of essentially unchanged drug stored without apparent damage to the host, in such tissues as the liver and lungs, which are also the most frequent sites of extraintestinal amebiasis: the drug is excreted slowly and mainly by way of the bile, thus giving prolonged fecal levels.

Excellent therapeutic results in human amebiasis with Biallylamicol have been reported previously by several investigators[5,11-14] using doses of 1½ to 2 gm. daily for five to seven days. Minimal side-effects were noted and consisted mostly of gastrointestinal reactions, skin reactions and rarely headache, vertigo and in only one patient[4] transient albuminuria.

Because of the excellent results reported with these dosages it was decided to give the first patients in this study 500 mg. three times a day. It was empirically decided to prolong the course of therapy to 14 days. This decision was made primarily because of previous experience with other drugs using the same rigid criterion of cure. As will be noted the criterion of cure used in this study was three successive negative stool checks. The first check was usually not obtained until about four weeks after cessation of Biallylamicol therapy. It was felt that this offered the advantage of whatever therapeutic benefits there may have been from the prolonged tissue concentrations and slow excretion of the drug. Second and third checks were obtained usually at monthly intervals.

As noted in the accompanying detailed charts the first four patients treated with Biallylamicol in dosages of 500 mg. three times daily for 14 days all had symptomatic improvement but none was cured. In fact, the first stool check after therapy was positive in each patient. Since there were no indications in available information of serious toxicity from Biallylamicol, it was decided thereafter to increase future dosage schedules to three grams daily (750 mg. four times a day) for ten days. Patient 4 received one course of the larger dosage as did most of the later patients. Despite the larger doses no serious toxic reactions occurred though treatment had to be discontinued in several patients. In patients 9 and 10 gastrointestinal irritation was excessive and even on a reduced dosage forced discontinuing further therapy with Biallylamicol. Patient 13 deteriorated while under therapy but the medication cannot necessarily be blamed. This patient was a colored man who had an acute ulcerative colitis with amebiasis and ultimately required ileostomy and colectomy. Patient 14 discontinued medication on the eighth day because of a maculo-papular rash

particularly marked on the face. Patient 16 was a girl 11 years of age who had to stop treatment on the seventh day due to a skin rash with urticaria.

Almost all of the patients experienced symptomatic improvement. Of 17 patients completing the prescribed course of Biallylamicol therapy using larger doses (15 patients 3 gm. daily for ten days and 2 patients 2 gm. daily for 14 days) four were cured with one course of treatment. Ten patients received a second course of Biallylamicol in 3 gm. daily doses for ten days. Patient 6 had to be disregarded since no follow-up was obtained after the second course of therapy. Patient 20 developed severe urticaria on the fourth day of her second course and had to discontinue treatment. Of the remaining eight who received a full course of treatment four were cured.

In studying the results it seems worthwhile pointing out that had only one posttreatment stool examination been used as a criterion of cure that there would have been 11 negatives of the 21 patients treated with 2 or 3 gm. daily doses (and 3 of the positives did not complete the prescribed course of therapy). Had the criterion of cure been limited to two stool checks then after a single course of 2 or 3 gm. daily doses for 10 days there would have been seven cures of the 21 patients so treated. It is obviously difficult to compare the therapeutic efficacy of various antiamebic drugs in humans unless the technics and criteria are similar and variables reduced to a minimum. In the present study three warm specimens were examined from each patient at each check and a patient was not presumed cured until there had actually been three negative specimens on three different occasions or usually a total of nine negative specimens.

The same criterion has been used for some years and has resulted in apparently lower cure rates for many other accepted antiamebic drugs than generally reported. For many years routine office treatment has been to prescribe a group of antiamebic drugs. Such a multiple treatment course has recently consisted of the administration of chloraquine diphosphate simultaneously with successive courses of fumagillin (Fumadil), diiodhydroxyquin (Diodoquin), and carbarsone. This program has resulted in a cure rate of approximately 60 per cent (12 out of 21 patients) after one such course. The multiple drug treatment of amebiasis is used by many clinicians and usually includes two or more of the different types of available antiamebics selected from the following groups:

1. Emetine hydrochloride, one of the oldest amebicides, is effective especially against the trophozoites, and primarily in extraintestinal infections. Its use is limited by its toxicity and necessity of parenteral administration. An emetine derivative, emetine bismuth iodide, has been used orally but is also toxic and accompanied by many reactions.

2. Various antimalarials have been found effective as amebicides and primarily in the extraintestinal phases of amebiasis. Chloraquine has been gener-

ally accepted as the drug of choice[3] though quinacrine (Atabrine), Amodiaquin and others have been tried.

3. The group of arsenical derivatives has been effective in intestinal amebiasis and has direct amebacidal action but is contraindicated where hepatic or renal damage is present. Carbarsone, acetarsone (Stovarol), glycobiarsol (Milibis), thiocarbarsone, arsthinol (Balarsen) and others are used but have no value in extraintestinal amebiasis.

4. The commonly used iodized compounds are chiniofon (Yatren), iodochlorhydroxyquin (Vioform), and diiodochlorhydroxyquin (Diodoquin). All have amebacidal action in intestinal amebiasis. Iodine sensitivity is the only contraindication.

5. The last major group of antiamebics can include almost all of the antibiotics. Wide use of some of these agents followed initial reports of unusually high cure rates but later study was somewhat disappointing. Included in a recent survey[15] were chlortetracycline, oxytetracycline, bacitracin, chloramphenicol, neomycin and fumagillin. Penicillin and the sulfonamides have helped in some patients and more recently erythromycin[16] has been used with success. Antibiotic residues[17] have also been recently reported of value. The majority of the antibiotics, however, have little direct amebacidal action. Their primary action may well be a change of environment detrimental to the amebae. Fumagillin is exceptional in that it is directly amebacidal even in extreme dilutions. It has, however, little or no extraintestinal benefit while some of the others are helpful in extraintestinal amebiasis.

Other drugs used by the writer at various times have included emetine hydrochloride, chiniofon, glycobiarsol (Milibis), thiocarbarsone, quinacrine (Atabrine) hydrochloride, chloretetracycline (Aureomycin), oxytetracycline (Terramycin), and erythromycin. The author has had no experience with arsthinol (Balarsen) which several investigators have found very effective[2,18]. Making any comparative analysis of the efficacy of various antiamebic drugs from reports of different investigators is very unreliable due to the variables in criteria of cure. While most of the groups of previously available antiamebics have a usefulness limited to certain phases of amebic involvement, it is important to again note that the drug Biallylamicol is effective in both intestinal and extraintestinal amebiasis.

While the results in this study of Biallylamicol are not spectacular, Biallylamicol has been found by the present investigator to be the best single therapeutic agent he has used for treatment of human amebiasis as measured by the criteria of cure outlined previously. The group of patients is too small to draw definite conclusions. It seems possible, however, to suggest from this study that the optimum dosage of Biallylamicol may be between 2 and 3 gm. daily for at least ten days with a second course given in three or four weeks. Or possibly a

TABL

Pt.	Age	Sex	Wt. in lbs.	Symptoms & Findings	Trophozoites	Previous Therapy
1–AB	32	F	159	10 years bloating, cramps, diarrhea (1-3/day), occ. blood	+	Yes
2–TN	36	M	149	3 years cramps, loose stools with attacks of increased diarrhea, rectal itching, bloating		No
3–FH	45	F	158	5 years diarrhea (4-12/day), blood and pus, cramps, rectal ulcerations	+	Yes
4–KM	51	M	164	3 years abdominal fullness, diarrhea (2-3/day), occ. vomiting, wt. loss, cramps	+	Yes
5–BC	33	F	178	3 years upper abdominal pain, attacks of diarrhea		Yes
6–GB	24	M	165	6 months diarrhea (6-7/day), rectal ulcerations, enlarged liver, cramps	+	Yes
7–MS	52	F	141	6 months cramps, intermittent diarrhea (2-7/day)	+	No
8–CJ	14	F	146	18 months bloody diarrhea (10-12/day), fever, weight loss, cramps	+	Yes
9–KJ	32	M	147	1-4 years cramps, diarrhea (1-3/day), rectal itching	+	No
10–GK	58	M	120	10 years cramps, diarrhea (1-3/day), occ. blood, flatus, amebic granuloma of sigmoid		Yes
11–HC	49	M	153	3 years cramps, intermittent diarrhea, rectal itching and burning, fatigue		Yes
12–DA	33	M	156	2 years cramps, intermittent nausea, vomiting and diarrhea, rectal itching, abdominal burning		No
13–MF	58	M	151	3 months bloody diarrhea (10-15/day), cramps, weight loss, vomiting, fatigue, fever		No
14–GP	38	F	123	3 months diarrhea (3-5/day), occ. blood, fever, weight loss, rectal itching	+	Treate in 1949-5
15–CH	34	M	140	2 months diarrhea (1-4/day), cramps, abdominal soreness	+	Yes
16–GF	11	F	90	6 months cramps, diarrhea (1-4/day), occ. blood		No
17–MP	38	F	120	9 months cramps, intermittent diarrhea	+	No
18–RF	53	M	167	1 year diarrhea (3-4/day), abdominal fullness, gaseous distress and flatus, eructation	+	No
19–BB	49	F	138	10 months cramps, diarrhea (2-4/day), frequent blood, fatigue, flatus, rectal ulcerations	+	Yes
20–HS	31	F	144	8 years cramps, diarrhea (5-6/day), fatigue, flatus, rectal ulcerations	+	Yes
21–NH	44	M	160	6 months cramps, diarrhea (1-3/day)		Yes
22–LW	55	F	132	6-7 years cramps, intermittent diarrhea, hyperacidity		Yes
23–LB	65	F	135	35 years diarrhea (1-4/day), cramps, bloating, flatus, enlarged liver	+	Yes
24–FH	45	F	158	5 years diarrhea, (3-10/day), frequent blood, cramps, rectal ulcerations	+	Yes
25–TB	23	M	132	3 years fatigue, intermittent diarrhea, weight loss		Yes

Results One Course						Results Second Course						
Daily Dosage	Improved Symptoms	Stool Check 1	Stool Check 2	Stool Check 3	Reaction	Dosage	Improved Symptoms	Stool Check 1	Stool Check 2	Stool Check 3	Reaction	Cured
1½ gm. 14 days	Yes	+			No							No
1½ gm. 14 days	Yes	+			No							No
1½ gm. 14 days	Yes	+			No							No
1½ gm. 14 days	Yes	+			No	3 gm. 10 days	Yes	0	+		Rash (face)	No
3 gm. 10 days	Yes	+			No							No
3 gm. 10 days	Yes	+			Slight Nausea	3 gm. 10 days	Yes				No	Uncooperative No follow-up
3 gm. 10 days	Yes	0	0	0	No							Yes
2 gm. 14 days	Yes	0	0	0	No							Yes
3 gm. 4 days 1½ gm. 4 days	No	+			Nausea & vomiting urticarial rash							No. Had to stop treatment
3 gm. 4 days 2 gm. 4 days	No	+			Increased cramps & diarrhea							No. Had to stop treatment
3 gm. 10 days	Yes	0	0	0	No							Yes
3 gm. 10 days	Yes	0	0	0	No							Yes
3 gm. 5 days 2 gm. 5 days	No	+			All symptoms worse							No
3 gm. 8 days	Yes	0	0	+	Severe face rash stopped on 8th day							No
3 gm. 10 days	Yes	0	0	+	No							No
1 gm. 14 days	Yes	+			Rash & hives 7th day							Stopped treatment 8th day
2 gm. 14 days	Yes	0	+		No	3 gm. 10 days	Yes	+			No	No
3 gm. 10 days	Yes	+			No	3 gm. 10 days	Yes	0	0	0	No	Yes
3 gm. 10 days	Yes	0	+		No	3 gm. 10 days	Yes	+			No	No
3 gm. 10 days	Yes	+			No	3 gm. 10 days					Severe hives 4th day	Had to stop treatment
3 gm. 10 days	Yes	+			No	3 gm. 10 days	Yes	0	+		No	No
3 gm. 10 days	Yes	0	0	+	No	3 gm. 10 days	Yes	0	0	0	No	Yes
3 gm. 10 days	Yes	0	+		No	3 gm. 10 days	Yes	+			No	No
3 gm. 10 days	Yes	+			No	2 gm. 14 days	Yes	0	0	0	No	Yes
3 gm. 10 days	Yes	+			Slight rash 10th day	2 gm. 14 days	Yes	0	0	0	No	Yes

single longer course of treatment would be more effective. Barrios[5] gave one patient 56 gm. of Biallylamicol without toxic effects during continuous therapy. Using 2 gm. of Biallylamicol daily for 21 to 28 days may finally be found to be the most effective dosage schedule. The writer believes most therapies are not carried out for a sufficient duration to cure the patient. Theoretically, if even one ameba remains viable after therapy in any patient, persisting infection with recurring symptoms is possible. Whether repeated heavier courses or more prolonged smaller doses will be found superior will depend on further study. The writer believes either plan of treatment with Biallylamicol will give a more satisfactory cure rate than here reported.

Summary of Clinical Results of Biallylamicol Therapy

In 36 courses of treatment with Biallylamicol given to 25 patients no serious toxic reactions occurred. In the 36 treatment courses five patients developed skin reactions which in three patients necessitated stopping the course of therapy. One patient (25) developed a skin rash at the end of the first course of treatment but later tolerated a lower dose without difficulty. Four patients had increased gastrointestinal disturbances which in two required cessation of Biallylamicol. Gastrointestinal complaints were minimized after the medication was prescribed with meals and with food at bed time.

Of nine patients (1,2,3,4,9,10,13,14, and 16) who received a total dosage of 24 gm. or less of Biallylamicol in a 7 to 14 day period none was cured. In 17 patients receiving from 28 to 30 gm. in a 10 to 14 day period, four were cured with one course of therapy. In eight patients who completed a second course of therapy of 28 to 30 gm. of Biallylamicol, administered three weeks or more after cessation of the first course, four or 50 per cent were cured. Of 17 patients who received one or two courses of 28 to 30 gm. each in a 10 to 14 day period, 8 were cured.

Conclusions

Biallylamicol is a new synthetic organic chemical which demonstrates definite amebacidal activity and is effective in both extraintestinal, as well as intestinal, phases of human amebiasis. The previously recommended daily dosage schedules of 1½ gm. for five to seven days appear inadequate. Larger doses, 28 to 30 gm. in a 10 to 14 day interval, cured nearly 50 per cent of the 17 patients with active amebic dysentery who received one or two courses of therapy. The highest cure rate occurred when the course of treatment was repeated after three or more weeks rest. No serious toxic reactions occurred in 36 treatment courses administered to 25 patients.

Additional clinical study will be necessary to determine the optimum dosage of Biallylamicol and its proper place in treating human amebiasis. When

the optimum dosage is determined then one can expect higher cure rates than has been herewith reported.

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THE EFFECT OF SPICE INGESTION UPON THE STOMACH*

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One of the problems of diet therapy in peptic ulcer disease is the impalatability of the diet with resultant lack of patient cooperation. Physicians have warned patients to avoid "spices and highly seasoned foods" without objective evidence to support the effect of different spices on the gastric mucosa and the healing time of peptic ulcer. These studies were undertaken to evaluate the effect of different types of spices, in the amounts commonly used, upon the stomach and peptic ulcer disease.

In 1932 Heupke[1] showed by acute experience in healthy humans that anis oil (10 gtts. in 300 c.c. saline) stimulated gastric acid secretion but that caraway oil (10 gtts.), nutmeg (0.5 gm.), mustard oil (1 gtt.) and pepper (0.5 gm.) either had no effect or, in fact, decreased gastric secretion. Frank[2] by tube feedings in humans demonstrated that coriander, garlic, marjoram, dill, sage, savory, rosemary, celery, thyme and caraway have no significant effect on the secretion of acid by the stomach (1 gm. in 100 c.c. water for 5 minutes). These findings were confirmed in similar work by Harth[3] who found no increase in gastric acidity.

Damrau and Ferguson[4] using x-ray and fluoroscopy, found that garlic relaxed the gastrointestinal tract and delayed gastric emptying.

Animal studies have yielded some conflicting reports. Rabinowitsch[5] demonstrated in Pavlov dogs that mustard, cinnamon and cloves were mild gastric secretory stimulants, while equivocal results were obtained with paprika, pepper, caraway and nutmeg. Sanchez and his co-workers[6] working with humans and with dogs showed that there was no effect on acid secretion with cinnamon, cloves, paprika and pepper (in amounts of 1 gm.) and that mustard definitely inhibited gastric acidity. In presenting their concept of the "gastric mucus barrier" the same authors applied cotton pledgets soaked with spices and saline to the gastrointestinal mucosa of dogs for three hours. Mustard, and to a lesser extent, paprika, pepper and cinnamon caused edema of the mucosa. Celery salt, cloves, nutmeg and sage had no effect. The intestinal mucosa was found to be "less resistant" to these agents than the gastric mucosa.

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Hollander[7] noted an increase in gastric secretion with mustard oil, but found that it consisted of a serous transudate with no increase in acid. Of all the spices studied, paprika has probably received the most attention. Varga[8] showed that this spice caused a mild increase in gastric acidity in normals, hypo- and hypersecretors. Berkesy[9], using three types of paprika, confirmed these findings and added the information that all three types of paprika had the same effect when administered for 30 minutes as a 11-13 per cent paprika extract.

Basing the conclusions empirically on clinical observations Heupke advised the elimination of all spices in acute gastrointestinal diseases, but permitted the use of cinnamon, bay leaf, vanilla and nutmeg in the ulcer regime, prohibiting curry, clove, garlic, paprika, mustard, pimento and onion.

TABLE I

Doses of Spice Administered to Ulcer Patients

	Spice	Dosage/Meal in gm.
1	Ground Cinnamon	0.90
2	Ground Nutmeg	0.30
3	Ground Jamaica Allspice	0.10
4	Ground West Indian Mace	0.15
5	Ground French Thyme	0.10
6	Ground Dalmatian Sage	0.25
7	Ground Spanish Paprika	0.30
8	Caraway Seed	0.2
9	Mustard Seed*	0.25
10	Cloves	0.05
11	Black Pepper	0.15
12	Chili Pepper	0.5

*Wet, ground mustard seed subsequently dried.

The evidence thus appears both incomplete and conflicting. In an attempt to evaluate the advisability of continuing the traditional prohibition of spices in the treatment of peptic ulcer disease the following study was undertaken.

Method

This investigation was divided into four parts:

I. *The Effect of Spices on the Clinical Symptomatology and Rate of Ulcer Healing:*—Fifty patients with active duodenal or gastric ulcer with demonstrable

TABLE II

EFFECT OF SPICES ON HEALING OF PEPTIC ULCER

Patient	Spice	Age	Sex	Diagnosis	Days on Spice	Healing Time (X-ray Evidence)	Symptoms
S.C.	Cinnamon	30	M	Duodenal ulcer gastritis	21	21 days	Belching and aftertaste when taken on an empty stomach; none when taken with meals
L.E.	Cinnamon	55	M	Duodenal ulcer	55	23-30 days	None
G.I.	Cinnamon	20	M	Duodenal ulcer	27	21 days	None
C.L.	Cinnamon	38	F	Duodenal ulcer	62	21-43 days	None
D.O.	Cinnamon	47	M	Chronic duodenal ulcer—gastritis	3		Heartburn if spice was taken between meals
J.A.	Nutmeg	40	M	Duodenal ulcer	39	43 days	None
C.O.	Nutmeg	40	M	Gastric ulcer	100	28 days	None when taken with meals; aftertaste and belching when taken after meals
S.M.	Nutmeg	47	M	Chronic duodenal ulcer	28	12 days*	None
G.A.	Nutmeg	69	M	Chronic duodenal ulcer—mild bleeding	61	28 days	t.i.d.—loose evacuations b.i.d.—none
B.E.	Nutmeg	52	M	Gastric ulcer	180	48 days	None
M.D.	Nutmeg	49	M	Duodenal ulcer	60	30 days*	None
D.O.	Nutmeg	34	M	Duodenal ulcer	50	50 days*	None
K.E.	Nutmeg	54	M	Duodenal ulcer	50	40 days*	None
S.I.	Nutmeg	70	M	Duodenal ulcer	12	12 days*	None
D.O.	Allspice	47	M	Chronic duodenal ulcer—gastritis	30	21 days*	None
C.A.	Allspice	53	M	Gastric ulcer	150	28 days*	Believes appetite increased by this capsule. Slight aftertaste when taken after meals; none with meals
E.D.	Allspice	72	M	Duodenal ulcer	65	21 days*	None
M.K.	Mace	53	M	Duodenal ulcer	30	30 days*	None
M.N.	Mace	51	M	Duodenal ulcer	75	20 days*	None
L.O.	Mace	49	M	Duodenal ulcer	55	14 days*	None
F.O.	Mace	46	F	Duodenal ulcer	60	30-64 days	Heartburn and aftertaste when taken on empty stomach; none with meals

*Clinical evaluation of healing time.

TABLE II (*continued*)

Patient	Spice	Age	Sex	Diagnosis	Days on Spice	Healing Time (X-ray Evidence)	Symptoms
T.O.	Mace	66	M	Duodenal ulcer	40	48 days	None
A.D.	Mace	43	M	Duodenal ulcer	90	15 days*	None
K.E.	Thyme	44	F	Duodenal ulcer	21	21 days	None
W.O.	Thyme	57	M	Duodenal ulcer	14	7 days*	None
D.A.	Thyme	44	M	Duodenal ulcer	60	12 days*	None
W.C.	Cloves		M	Duodenal ulcer	30	14 days*	Rare nausea
W.M.	Cloves	48	F	Duodenal ulcer	30	30 days*	None
P.A.	Cloves	14	M	Duodenal ulcer	60	21 days*	None
J.P.	Cloves	41	M	Duodenal ulcer	55	25 days*	None
M.C.	Mustard	65	F	Duodenal ulcer	35	30 days	None
E.C.	Mustard	31	M	Duodenal ulcer	28	28 days*	Rare nausea occasional heartburn
E.S.	Mustard	49	F	Duodenal ulcer	77	30 days* 60 days	None
I.C.	Mustard		F	Duodenal ulcer	28	30 days	None
J.M.	Black Pepper	43	M	Duodenal ulcer	3	—	Reactivation of marked ulcer pains in one day
S.P.	Black Pepper	53	F	Duodenal ulcer	1	—	Reactivation of all ulcer symptoms in one day
A.D.	Chili Pepper	36	F	Duodenal ulcer	55	28 days* 50 days	None
E.C.	Chili Pepper	35	M	Duodenal ulcer	14	14 days*	None
M.S.	Chili Pepper	51	F	Duodenal ulcer	70	30 days*	Considerable heartburn after 60 days. Symptoms cleared when spice discontinued
M.J.	Caraway Seed	34	F	Gastric ulcer	56	56 days	None
S.P.	Caraway Seed	46	M	Duodenal ulcer	35	35 days*	None
M.S.	Caraway Seed	56	F	Duodenal ulcer	42	42 days*	None
C.P.	Caraway Seed	66	M	Duodenal ulcer	42	42 days*	None
C.H.	Caraway Seed	59	M	Duodenal ulcer	28	28 days*	None
E.M.	Paprika	59	F	Gastric ulcer	28	21 days	None
M.H.	Paprika	67	F	Gastric ulcer	30	30 days* 60 days	None
R.E.	Paprika	28	M	Duodenal ulcer	35	35 days	None
A.A.	Sage	66	M	Duodenal ulcer	28	28 days	None
E.A.	Sage	39	M	Duodenal ulcer	35	35 days	None
E.B.	Sage	48	M	Duodenal ulcer	42	42 days	Slight aftertaste

*Clinical evaluation of healing time.

craters by x-ray were maintained on a routine ulcer regimen including a progressive ulcer diet, interval feedings, antispasmodics, and antacids. They were given, in addition, a capsule containing a spice, the nature of which was unknown to the patient, three times daily with meals. The spices tested included cinnamon, nutmeg, allspice, mace, thyme, sage, paprika, caraway seed, chili pepper, cloves, black pepper, and mustard seed. The amount of each spice administered was estimated according to the maximum amount used in some of the more highly spiced recipes appearing in the "ABC of Spice Cookery", published by The American Spice and Trade Association[10]. The dosage per meal for each spice is presented in Table I. The spices were administered in

TABLE III

EFFECT OF SPICES ON INACTIVE DUODENAL ULCER NOT ON ROUTINE ULCER REGIMEN

Patient	Spice	Age	Sex	Diagnosis	Days on Spice	Symptoms
H.M.	Cloves	70	M	Duodenal Ulcer	14	Considerable belching ½ hr. p.c.
H.M.	Cloves	70	M	Duodenal Ulcer	14	Considerable belching ½ hr. p.c. on ulcer regimen; clearing when drug was discontinued
J.S.	Cloves	68	M	Duodenal Ulcer	42	None
A.M.	Mustard	43	M	Duodenal Ulcer	14	None
T.C.	Mustard	53	M	Duodenal Ulcer	30	None
A.B.	Black Pepper	50	F	Duodenal Ulcer	3	Heartburn, belching very marked after 2 days of spice
T.C.	Chili Pepper	53	M	Duodenal Ulcer	30	None
B.G.	Chili Pepper	37	M	Duodenal Ulcer	28	None

doses of 0.05–0.9 gm. three times daily for an average of 40 days, the dosage depending upon the individual spice administered.

The patients were closely questioned regarding untoward symptoms from these capsules with special emphasis upon heartburn, after-taste, indigestion, belching or pain. Each patient was evaluated at frequent intervals in respect to clinical response to therapy. X-rays were repeated at varying periods, and the healing time was estimated in each patient either clinically or by x-ray evidence (Table II).

II. *The Effect of Spices on the Clinical Symptomatology of Inactive Peptic Ulcer Patients Not on a Routine Ulcer Regimen:*—This group of asymptomatic patients with chronic duodenal ulcer, evidenced by duodenal deformity without a demonstrable crater, were taken off the usual ulcer regimen or interval feed-

ings, antacids and antispasmodics and were allowed only a moderately bland diet three times daily and a spice capsule with meals (Table III).

III. *The Gastroscopic Appearance of the Stomach Before and After the Ingestion of Spices:*—Fifteen patients were gastroscoped before and after the

TABLE IV

EFFECT OF SPICES UPON THE GASTROSCOPIC APPEARANCE OF THE STOMACH

Spice	Patient	Appearance Before Spice	Amount of Spice for 10 Min.	Appearance After Spice	Effect
Cinnamon	E.Y.	Gastric ulcer—atrophic gastritis	0.75 gm.	No change	None
Nutmeg	C.A.	Two large gastric ulcers and severe hypertrophic gastritis	0.75 gm.	No change	None
Allspice	G.A.	Normal mucosa	0.25 gm.	No change	None
Mace	C.A.	Healing gastric ulcers	0.37 gm.	No change	None
Thyme	L.A.	Hypertrophic gastritis	0.25 gm.	Very mild hyperemia	Mild irritant
Mustard	E.R.	Entirely normal mucosa	0.63 gm.	Very mild hyperemia	Mild irritant
Black Pepper	B.B.	Entirely normal mucosa	0.37 gm.	Marked hyperemia	Strong irritant
Black Pepper	A.A.	Moderate hypertrophic gastritis of antral area, otherwise normal	0.37 gm.	Considerable beefy redness of antral area which bled easily with instrumentation; remainder of stomach also appeared very hyperemic	Strong irritant
Chili Pepper	D.O.	Entirely normal mucosa	1.25 gm.	Moderate hyperemia	Mild irritant
Chili Pepper	J.S.	Chronic hypertrophic gastritis	1.25 gm.	Moderate increase in superficial hyperemia	Mild irritant
Cloves	C.A.	Entirely normal mucosa	0.125 gm.	No change	None
Cloves	F.K.	Chronic hypertrophic gastritis with superficial hyperemia	0.125 gm.	No change	None
Cloves	C.C.	Entirely normal mucosa	0.125 gm.	No change	None
Paprika	E.M.	Normal mucosa	0.75 gm.	No change	None
Paprika	S.S.	Normal mucosa	0.75 gm.	No change	None

instillation of spices into the stomach through an Ewald tube. The color and general appearance of the gastric mucosa was determined before and after contact with the spice solution. Solutions of spice were prepared containing two and one-half times the single dosage of spice mixed in 30 c.c. of water. This solution was introduced into the stomach and the patient slowly rolled from

side to side for ten minutes. The gastric contents were then aspirated and gastroscopic observations carried out.

IV. *The Effect of Spices on Gastric Secretion of Pepsin:*—The effect of spices on gastric secretion of pepsin was determined by measuring the uropepsin excretion in the urine before and after the ingestion of spices, by a modified method of Bucher, Anson and Mirsky[11].

Results

Fifty patients with active peptic ulcer maintained on an ulcer regime were given either cinnamon, nutmeg, allspice, mace, thyme, sage, paprika, caraway seed, chili pepper, cloves, black pepper, or mustard seed in doses of .05 to .9 gm. three times daily with meals for periods up to 180 days. Only five patients in this group developed symptoms during the administration of spices: two with

TABLE V

Uropepsin Excretion Before and After Spice Ingestion

Spice	Name	Spice Administration (Days)	Uropepsin Units/24 hours	
			Pre-Spice	Post-Spice
Cinnamon	S.C.	21	13,042	13,500
Nutmeg	B.E.	37	6,140	6,600
Allspice	P.E.	25	719	750
Allspice	D.O.	30	6,500	6,850
Cloves	P.O.	55	10,750	12,663

black pepper, one with chili pepper, one with nutmeg and one with mustard seed.

One patient (C.O) reported an after-taste and "heartburn" when the spice was ingested after the meal (Table II). This patient stated that nutmeg taken immediately after meals produced a "sour acidity taste"; if taken in the middle or the beginning of the meal, there were no symptoms. This patient had a large gastric ulcer as well as a duodenal ulcer. He was maintained on nutmeg in doses of .3 gm. three times daily for 100 days and remained completely asymptomatic as long as he took the spice in the middle of the meal or the beginning of the meal. His ulcer was no longer visualized by x-ray after 28 days, which is the anticipated average healing time without spice[12,13].

Patient M.S. with peptic ulcer remained asymptomatic while taking chili pepper three times daily for two months but noted a burning sensation and "heartburn" at the end of the second month, which disappeared when chili

pepper was omitted. The other patients maintained on chili pepper or nutmeg for one to three months remained asymptomatic. Mustard seed produced occasional nausea and heartburn in patient E.C. while maintained on the spice for 28 days.

Black pepper was administered to two patients who developed severe burning epigastric pain, belching, and nausea within 24 hours, requiring discontinuation of the spice. Black pepper was not administered further because of the severity of symptoms.

Several other patients reported heartburn, after-taste or belching when the spice was taken on an empty stomach. This applied to cinnamon, nutmeg, allspice and mace (Table II). Two patients claimed that the capsules (nutmeg) increased their appetite, and another noted that the capsules (nutmeg) helped regulate his bowel movements.

As far as can be determined, the spices enumerated above, with the exceptions already described, did not exert an injurious effect and did not alter the healing time of the peptic ulcer as determined clinically or by repeated x-rays of the stomach, before, during and after the administration of spices. The patients became rapidly asymptomatic during the simultaneous ulcer management and spice administration, and the ulcer healed by x-ray criteria or clinically in four to eight weeks in all instances. This does not differ from the anticipated healing time of other series of patients on a similar ulcer regimen without the administration of spices[12,13].

Patients with inactive duodenal ulcer who were not maintained on an ulcer regime were given cloves, mustard seed, black pepper and chili pepper (Table III). One patient taking cloves developed considerable belching one-half hour after meals. These symptoms disappeared when the spice was discontinued and the patient placed on an ulcer regimen. The symptoms recurred, however, when cloves were reinstituted, although the patient was maintained on the ulcer regime. Another patient developed marked symptomatology after two days of black pepper administration, and this spice was discontinued in three days. The remainder of the patients remained asymptomatic despite the fact that they did not receive interval feedings, antispasmodics or antacids.

Gastroscopically there was no significant change in the mucosa of 15 patients tested with cinnamon, nutmeg, allspice, thyme, black pepper, chili pepper, cloves and paprika. The dose of spices injected into the stomach was two and one-half times the amount used in highly seasoned food. For technical and practical reasons the length of contact of the spice solution with the empty stomach was ten minutes. Thyme and mustard seed produced a mild erythema but no symptoms. Chili pepper appeared to be a somewhat stronger irritant producing a moderate hyperemia of the mucosa. Black pepper, however, induced a severe hyperemia of the gastric mucosa, although no symptoms were

noted during the administration of these spices. The other spices tested produced no change in the color or appearance of the mucosa (Table IV).

The uropepsin excretion which measures the gastric pepsin, and usually parallels the hydrochloric acid excretion[14] remained essentially unchanged after 21 to 55 days of spice administration. It would appear that cinnamon, nutmeg, cloves, and allspice do not alter gastric pepsin secretion when administered daily for periods up to 55 days (Table V).

Discussion

The spices which appear to be associated with gastric distress when taken with food are black pepper, chili pepper, mustard seed, and cloves. In one instance nutmeg taken after meals produced epigastric distress. The frequency with which the spices produced epigastric distress when taken on an empty stomach suggest that food buffers the irritant effect of spices upon the gastric mucosa.

It should be emphasized that the 50 ulcer patients receiving the spices were maintained on the usual ulcer regime including significant amounts of antacids, and that these antacids may in part counteract the irritating effect of spice ingestion. The spices, however, with the exception of those noted above, did not appear to alter the healing time of the ulcer.

The dose of spice administered was determined by its usage in highly spiced recipes (Table I). Four slices of cinnamon toast, for example, requires approximately .9 gm. of cinnamon. The patients were thus given .9 gm. of this spice three times daily.

Black pepper and chili pepper which produced the most severe epigastric distress also induced the most marked changes gastroscopically, although thyme and mustard seed produced gastric erythema as well.

In the presence of gastritis black pepper may produce a marked aggravation of the inflammation as noted in Patient A.A. (Table IV), where an area of pre-existing hypertrophic gastritis of the antrum presented a beefy red mucosa with bleeding after the introduction of black pepper.

The absence of an increase in uropepsin during spice administration does not exclude an irritating effect.

From these studies it would appear that cinnamon, allspice, mace, thyme, sage, paprika and caraway seed administered with food does not exert a harmful effect upon the stomach, and may be innocuous in the amounts used, although the number of patients studied with each spice is limited. Black pepper, chili pepper, mustard seed and probably nutmeg and cloves may be considered gastric irritants.

Conclusions

1. Cinnamon, allspice, mace, thyme, sage, paprika, and caraway seed administered to peptic ulcer patients, under treatment with an ulcer diet, interval feedings, antacids and antispasmodics did not appear to alter the healing time of the ulcer crater when given in relatively large amounts with food three times daily over a period of two weeks to five months.

2. No untoward symptoms such as heartburn, indigestion, belching or pain were observed if these spices were ingested with food.

3. Symptoms such as heartburn, after-taste, belching or epigastric distress often occurred if the spices were taken on an empty stomach. This applies to all spices studied.

4. Black pepper and cloves produced epigastric symptoms in patients with inactive duodenal ulcers who ingested the spices with meals, but who were not maintained on the usual ulcer regimen.

5. Black pepper, chili pepper, cloves, mustard seed and probably nutmeg may be considered gastric irritants.

6. Black pepper and chili pepper which produced symptoms also induced the most marked hyperemia and edema of the gastric mucosa observed gastroscopically. Thyme and mustard seed produced gastric erythema.

7. The uropepsin excretion was not altered by spice ingestion.

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USE OF SILICONE ANTIFOAM IN GASTROSCOPY

MARK W. GARRY, M.D.

Milwaukee, Wisc.

The occurrence of bubble formation or frothy secretions in the stomach during gastroscopic examination is quite annoying. While it is not a factor in a large percentage of the patients examined, its presence in those cases requiring the most critical appraisal of the entire mucosal surface can be particularly serious.

When information became available concerning the use of silicones with defoaming properties[1,2], a supply of one of the materials, XEC 151*, was obtained from the manufacturer[3]. This was a white liquid substance of heavy creamy consistency, tasteless, and with a mild, inoffensive aroma.

Initially, the undiluted XEC 151 Emulsion was administered according to the method recommended by Hirschowitz, et al[1]. This was soon abandoned because an unpredictable portion of the total amount of the material was de-

TABLE I

WITH XEC 151

TOTAL PATIENTS—200

No Bubbling	+	++	+++
192	8	0	0

livered to the stomach and the flow of the emulsion through the esophagus was unduly prolonged. Several alternate procedures were then employed, using undiluted and varying dilutions of the material.

The method finally decided upon has been employed for the past year and this report concerns the results of its use in 200 patients compared with 200 patients in whom it was not used.

Preoperative medication consists of sodium luminal, gr. II, and atropine sulfate, gr. 1/100, subcutaneously, one hour before, and Demerol, 50 to 100 mg., subcutaneously, depending upon age, one-half hour before gastroscopy. Cocaine 4 per cent is applied directly by cotton pledget to the lateral pharyngeal wall above the pyriform sinuses. Three to five minutes later the gastric secretions are evacuated by intubation. Following withdrawal of the tube, another smaller tube, 0.4 cm. in diameter and 26.0 cm. in length, is introduced into the eso-

Department of Medicine, Veterans Administration Hospital, Wood, Wisc., and Marquette University School of Medicine, Milwaukee, Wisc.

*XEC 151 (Dymasyl) was kindly supplied by Mr. A. William Rhodes, Research Department, Dow Corning Corporation, Midland, Mich.

phagus. Silicone antifoam XEC 151, 1 c.c., is mixed with 1 c.c. of water and drawn into a 10 c.c. syringe. This mixture is instilled into the esophagus through the tube, followed by 10 c.c. of air; the tube is withdrawn and the patient is asked to swallow.

The amount of bubbling was arbitrarily graded as one, two or three plus, if it was slight, moderate, or extensive, respectively. Table I summarizes the result of the study of 200 patients receiving the silicone antifoaming agent prior to gastroscopy. Table II presents the findings in a control group of 200 patients without silicone.

It will be noted that, of the control group, 16 patients, or 66 per cent of the total number showing some degree of bubbling, had sufficient bubbling to seriously limit or wholly invalidate gastroscopic observation.

Of the prepared group, only eight revealed any bubbling and this was so slight as to be inconsequential.

TABLE II

WITHOUT XEC 151

TOTAL PATIENTS—200

No Bubbling	+	++	+++
176	8	6	10

Of equal interest were the observations that the antifoaming agent was nontoxic, did not interfere with the interpretation of mucosal appearance and caused no apparent reaction of the mucosa.

SUMMARY

1. Evaluation of the use of a silicone antifoaming agent XEC 151 Emulsion in 200 gastroscopic examinations, when compared with a control group of 200 patients examined without the silicone preparation, demonstrates its effectiveness in eliminating a significant degree of bubbling.

2. A consistently effective method of administration has been described which employs only a small amount of the silicone emulsion with entirely satisfactory results.

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President's Message

Successful Conventions

Conventions are often uninteresting and boring. Our convention in New York was interesting and exciting from the beginning to the end. The six medical schools of New York cooperated with us in giving us the best of the latest in Gastroenterology.

The Postgraduate Course was almost as interesting as the regular convention. The attendance at both was remarkable and spoke well for the fine efforts of our Program Committee headed by Dr. Frank J. Borrelli.

The scientific exhibits were the largest ever and the pharmaceutical demonstrations exceeded anything to date. Much credit should go to Dr. Michael W. Shutkin and his committee for their fine efforts.

There is a special dividend often overlooked for those who attend our convention regularly. It is the fellowship which leads to everyone knowing each other by name. Plan now for the Boston convention next October and claim your membership dividends.

My heartfelt thanks to all who made the past convention such a success.

Arthur A. Kirchner

EDITORIAL

Silver Anniversary Year

This month the American College of Gastroenterology starts its Silver Anniversary Year. It was in December of 1932 that a certificate of incorporation was issued in New York State to the Society for the Advancement of Gastroenterology, which had held its incorporation meeting the previous month at the home of Dr. Samuel Weiss.

From a local organization, which quickly became a national group within two years, has emerged the largest gastroenterological association in the world. Accompanying this growth were three changes in name, including that to the American College of Gastroenterology in 1954.

Although the College is in existence 25 years it did not hold its first convention until 1936. One of the very first projects undertaken by the infant society was the quarterly publication of an official journal called The Review of Gastroenterology. This periodical, the pioneer journal of gastroenterology, proctology and allied subjects in the United States and Canada, matched the expansion of the organization, becoming a monthly journal with a change of name to The American Journal of Gastroenterology and a list of subscribers in all parts of the globe.

The Annual Conventions and more recently the Courses in Postgraduate Gastroenterology of the American College of Gastroenterology, are the foremost meetings in this field in the United States. Under the leadership of such outstanding men as Anthony Bassler, Roy Upham, G. Randolph Manning, William Reid Morrison, C. J. Tidmarsh, to name but a few, the size and the influence of the College in medical circles has steadily increased.

With new leaders, new ideas and a devotion to the organization and what it stands for, we hope to make the next 25 years in gastroenterology as praiseworthy, as full and as rich as have been these, our first 25 years.

NEWS NOTES

Future College Meetings

In response to numerous requests for information concerning dates and places of future meetings of the American College of Gastroenterology, we list:

Regional Meeting, Grand Rapids, Mich., March or April 1957.

22nd Annual Convention, Boston, Mass., 20-26 October 1957.

23rd Annual Convention, New Orleans, La., 19-25 October 1958.

24th Annual Convention, Los Angeles, Calif., 20-26 September 1959.

25th Annual Convention, Philadelphia, Pa., 23-29 October 1960.

26th Annual Convention, Chicago, Ill. (tentative), 22-28 October 1961.

College Officers for 1956-1957

Dr. C. Wilmer Wirts of Philadelphia, Pa., was chosen as president-elect of the American College of Gastroenterology at the Annual Meeting of the College held Sunday, 14 October in New York. He will assume the Presidency at the Annual Meeting to be held in Boston, Mass., October 1957.

Dr. Arthur A. Kirchner of Los Angeles, Calif., who became president-elect in Chicago in 1955, assumed the presidency of the College at the Annual Banquet held at The Roosevelt on Tuesday evening, 16 October. He succeeds Dr. James T. Nix of New Orleans, La.

Other officers elected were: Vice Presidents, Drs. Frank J. Borrelli, New York, N. Y.; Joseph Shaiken, Milwaukee, Wisc.; Henry Baker, Boston, Mass. and Louis Ochs, Jr., New Orleans, La. Dr. Theodore S. Heineken of Bloomfield, N. J. was re-elected Secretary.

Elected trustees are Drs. H. Necheles, Chicago, Ill.; Louis L. Perkel, Jersey City, N. J.; M. E. Steinberg, Portland, Oregon; Murrel H. Kaplan, New Orleans, La.; Milton J. Matzner, Brooklyn, N. Y. and John M. McMahon, Bessemer, Ala.

The following were elected governors: Drs. Henry A. Monat, Washington, D. C.; Harry A. Oberhelman, Chicago, Ill.; Sam A. Overstreet, Louisville, Ky.; Charles W. McClure, Boston, Mass.; James A. Ferguson, Grand Rapids, Mich.; Earl J. Halligan, Jersey City, N. J.; Libby Pulsifer, Rochester, N. Y.; William L. Leet, Providence, R. I.; Henry G. Rudner, Sr., Memphis, Tenn. and Robert T. McCarty, Milwaukee, Wisc.

Dr. Henry G. Rudner, Sr., Memphis, Tenn., was chosen by the governors to be their new chairman and Dr. James T. Nix was elected by the trustees as chairman of the Board of Trustees.

At their first meeting, the Board of Trustees appointed Dr. Lynn A. Ferguson of Grand Rapids, Mich., as Secretary-General to succeed the late Dr. Roy Upham and Dr. William C. Jacobson, New York, N. Y., Treasurer to succeed the late Dr. Elihu Katz. Dr. Robert R. Bartunek of Cleveland, Ohio was appointed trustee for one year to replace the late Dr. Samuel S. Berger and Dr. Harry Barowsky, New York, N. Y., was appointed a trustee for one year to replace Dr. Jacobson. Dr. Samuel Weiss, New York, N. Y., was reappointed Editor-in-Chief of the official publication, THE AMERICAN JOURNAL OF GASTROENTEROLOGY.

Arthur A. Kirchner, M.D., F.A.C.G., incoming President *(left)* receiving the President's insignia from James T. Nix, M.D., F.A.C.G., the outgoing President, at the Annual Banquet of the American College of Gastroenterology, Hotel Roosevelt, New York City, 16 October 1956.

Dr. Arthur A. Kirchner, President, appointed Dr. Irving A. Levin of New Orleans, La., to succeed Dr. Louis Ochs, Jr., Dr. Stanley Sidenberg of Cleveland, Ohio to succeed Dr. Robert R. Bartunek and Dr. Samuel W. Yabroff, San Francisco, Calif. as governors for their respective states and areas.

1956 AMES AWARDS

The American College of Gastroenterology takes pleasure in announcing that the first prize and a Certificate of Merit in its 1956 Ames Award Contest

for the best unpublished paper in gastroenterology, by a Fellow in gastroenterology, has been awarded to Dr. Samuel Katz of Chicago, Ill.

Dr. Katz, who originally comes from Buenos Aires, Arg., was with the Department of Gastrointestinal Research, Medical Research Institute of Michael Reese Hospital, Chicago, Ill. and the Department of Medicine of the University of Chicago. He is a Fellow of the Gustavus and the Louise Pfeiffer Research Foundation and the Inter-American Foundation for Postgraduate Education.

The subject of his prize winning paper, which he presented at the closing session of the American College of Gastroenterology, on Wednesday evening, 17 October 1956, at The Roosevelt, is "Characteristics of Fat Splitting Enzymes in Health and Disease".

The second prize and a Certificate of Merit has been awarded to I. N. Marks of Edinburgh, Scotland, Medical Registrar of the Gastrointestinal Unit, Western General Hospital in Edinburgh and at present a Research Fellow at the Fels Research Institute in Philadelphia, Pa.

The subject of his paper was, "The Significance of the Gastric Secretions After Partial Gastrectomy and Gastroenterostomy".

The award for the best paper published during the past year in THE AMERICAN JOURNAL OF GASTROENTEROLOGY, the official publication of the American College of Gastroenterology, was given to Dr. George B. Jerzy Glass and Marilyn Rich of New York City for their paper, "Comprehensive Testing of Gastric Secretory Function". Dr. Glass is a Fellow of the College and Associate Professor of Medicine at the New York Medical College. Miss Rich is Research Assistant in the Gastroenterology Research Laboratory of the New York Medical College.

The presentation of the awards is to be made by Dr. Henry G. Rudner, Sr., a member of the Research Committee of the American College of Gastroenterology, at the Annual Banquet of the College.

INTERNATIONAL ACADEMY OF PROCTOLOGY 1956-1957 AWARD CONTEST

The International Academy of Proctology announces its Annual Cash Prize and Certificate of Merit Award Contest for 1956-1957. The best unpublished contribution on proctology or allied subjects will be awarded $100.00 and a Certificate of Merit. Certificates will be awarded also to physicians whose entries are deemed of unusual merit. This competition is open to all physicians in all countries, whether or not affiliated with the International Academy of Proctology. The winning contribution will be selected by a Board of impartial judges, and all decisions are final.

The formal award of the First Prize, and presentation of other Certificates, will be made at the Annual Convention Dinner Dance of the International Academy of Proctology, 2 May 1957, at The Plaza, New York, New York.

The International Academy of Proctology reserves the exclusive right to publish all contributions in its official publication, "The American Journal of Proctology". All entries are limited to 5,000 words, must be typewritten in English, and submitted in five copies. All entries must be received no later than the first day of February, 1957. Entries should be addressed to the International Academy of Proctology, 147-41 Sanford Avenue, Flushing, New York.

In Memoriam

We record with profound sorrow the passing of Dr. Sidney Lechner of Yonkers, N. Y., Fellow and Dr. H. C. Rutherford Darling of Sidney, New South Wales, Australia, Life Fellow of the American College of Gastroenterology. We extend our deepest sympathies to the bereaved families.

ABSTRACTS FOR GASTROENTEROLOGISTS

ESOPHAGUS

VARICES OF THE DISTAL ESOPHAGUS IN THE APPARENT ABSENCE OF PORTAL AND OF SUPERIOR CAVAL HYPERTENSION: Eddy D. Palmer and Irving B. Brick. Am. J. M. Sc. 230:515-518 (Nov.), 1955.

The authors discuss idiopathic varices of the distal esophagus which exists without evidence of portal or superior caval hypertension. They point out that the absence of other clinical signs of venous hypertension is not necessary proof of normal portal or caval pressure. The difficulties of the diagnosis are discussed. The authors discuss 350 cases of esophageal varices, with particular emphasis on 13 cases of varices of the distal esophagus without venous hypertension. Nine of the 13 patients had bleeding; 8 of the 9 were found also to have associated esophagitis. This study led to the conclusion that varices of the distal esophagus develop and exist in the absence of portal and superior caval hypertension. These 13 cases represent 3.7 per cent of the total number of patients studied esophagoscopically. It was considered that esophagitis is the probable cause for initiation of hemorrhage of those esophageal varices which did bleed.

Bernard Farfel

ESOPHAGITIS, HIATUS HERNIA, AND CARDIOSPASM: David P. Boyd. A.M.A. Arch. Int. Med. 96:721 (Dec.), 1955.

Medical treatment of esophagitis with its complications is useful only in the milder cases. Here, in addition to diet and drugs, the patient can be taught to perform the dilations himself twice a week. However, advanced undilatable stricture requires surgical help. After a period of three months with preliminary gastrostomy and jejunostomy to correct nutritional deficiences, radical surgery is indicated in the form of resection of the middle and lower third of the esophagus and the upper third, which is more immune to inflammation and ulceration, is anastomosed to the fundus after closure of the cardia. Pyloroplasty or gastroenterostomy must be added to prevent

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ABSTRACTS FOR GASTROENTEROLOGISTS

ESOPHAGUS

VARICES OF THE DISTAL ESOPHAGUS IN THE APPARENT ABSENCE OF PORTAL AND OF SUPERIOR CAVAL HYPERTENSION: Eddy D. Palmer and Irving B. Brick. Am. J. M. Sc. 230:515-518 (Nov.), 1955.

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BERNARD FARFEL

ESOPHAGITIS, HIATUS HERNIA, AND CARDIOSPASM: David P. Boyd. A.M.A. Arch. Int. Med. 96:724 (Dec.), 1955.

Medical treatment of esophagitis with its complications is useful only in the milder cases. Here, in addition to diet and drugs, the patient can be taught to perform the dilations himself twice a week. However, advanced undilatable stricture requires surgical help. After a period of three months with preliminary gastrostomy and jejunostomy to correct nutritional deficiences, radical surgery is indicated in the form of resection of the middle and lower third of the esophagus and the upper third, which is more immune to inflammation and ulceration, is anastomosed to the fundus after closure of the cardia. Pyloroplasty or gastroenterostomy must be added to prevent

acid regurgitation. Apart from the surgical treatment of intractable cases, surgery is required in the presence of severe hemorrhage or perforation. Under these circumstances there is no standardized therapy and the surgical intervention must be individualized.

H. B. EISENSTADT

REGURGITANT ESOPHAGEAL ULCER: Herbert W. Schmidt. A.M.A. Arch. Int. Med. 96:717 (Dec.), 1955.

Regurgitant ulcer of the esophagus occurs most frequently with congenital or acquired hiatus hernia but it also can be observed after esophageal surgery altering the function of the pinchcock mechanism. In addition, it may be observed in various patients with intractable vomiting, for instance, due to obstructive gastric or duodenal lesions or in nervous persons with hypersensitive gag reflex.

Symptoms consist of dysphagia which is intermittent in spastic obstruction and continuous in organic narrowing, of retrosternal burning, epigastric pain, pyrosis, vomiting, hemorrhage and weigh' loss.

Diagnosis is made by x-ray examination showing a constricted segment with or without an ulcer niche. Esophagoscopy must be always added in order to exclude malignancy.

Treatment of regurgitant esophageal ulcer is unsatisfactory. Medical therapy consists of an ulcer regime with antispasmodics and antacids and of dilatation with sounds.

H. B. EISENSTADT

STOMACH

ASPIRIN AND GASTRIC HEMORRHAGE: A. P. Waterson. Brit. M. J. 4955:1531 (24 Dec.), 1955.

The author calls attention to Muir and Cossar's observation in 1955 to the effect that one-third of the patients with peptic ulcer and about one in twenty of a series of controlled patients complained of dyspepsia after taking aspirin, suggesting that in one in eight cases of hematemesis aspirin had been "at least the contributory cause" of the bleeding.

In every large series of cases of hematemesis and melena there are some which defy diagnosis in spite of every investigation including laparotomy and postmortem examination. It is urged that all bleeders be questioned carefully as to their aspirin habits in order to discover whether any cases might reasonably be attributed to the drug alone. In the author's series of 165 patients it was found that in three cases there was reasonably good evidence that aspirin was the causative factor in hemorrhage. He advocates the use of calcium aspirin or enteric coated tablets when it is certain that aspirin must be given to patients who have minor gastrointestinal symptoms when the drug is taken.

JOHN E. COX

A STUDY OF HIATAL HERNIAE, USING PNEUMOPERITONEUM: Wilbur C. Berry, John P. Holbrook, Edward A. Langdon and Carleton W. Mathewson. U.S. Armed Forces M. J. 6:1715 (Dec.), 1955.

Accurate evaluation of upper abdominal symptoms in the presence of a roentgenologic evidence of diaphragmatic hiatal hernia can be very difficult. Esophageal hiatus hernia is not only the "masquerader of the upper abdomen" but very often of the chest also.

In order to determine those cases which might be improved or cured by operation a pneumoperitoneum was produced in ten patients in whom a diagnosis of hiatus hernia was made. All of these cases were imroved by this procedure. Following repair of their hiatus herniae all showed postoperative improvement closely correlated with the degree of improvement gained by the pneumoperitoneum. The mechanism by which relief is obtained is not entirely clear though it is believed that pneumoperitoneum reduces the hernia.

ALEXANDER ZABIN

INTESTINES

PROLAPSE OF THE RECTUM: T. H. Thomason. Med. Times, 83:1026, (Oct.), 1955.

According to the author true rectal prolapse is a real hernia, where all the coats of the large bowel are prolapsed through the anal sphincter. This is a very rare and disabling disease. It should not be confused with rectal protrusion. The true prolapse, most probably caused by weakness of the rectal wall, represents all the burdensome problems of a hernia and should be surgically treated. Three methods are discussed: 1. the winding of a rubberband around the prolapse, 2. the surgical repair from below, and 3. the method the author prefers to do, namely the repair and fixation from an abdominal incision. This surgical procedure is outlined in detail and illustrated on two cases, the author has operated upon successfully.

HANS J. JOSEPH

NONMALIGNANT GRANULOMATOUS LESIONS OF THE RECTOSIGMOID: Irving Rapfogel. Am. Pract. & Digest Treat., 6:1495, (Oct.), 1955.

By granulomatous lesion is meant any proliferative or inflammatory lesion that produces or is capable of producing granulomatous tissue or tumorous swelling or masses. These lesions may resemble characteristic cancerous lesions grossly; in addition polypoid degeneration, such as occurs in ulcerative colitis and gonorrheal proctitis, may be a precancerous lesion. The lesions which the author considers are: 1. Chronic hypertrophic proctitis. This occurs in debilitating conditions, such as diabetes mellitus, chronic cardiovascular and liver disease. It is due to a variety of bacterial invaders. 2. Radiation proctosigmoiditis seen usually in patients who have undergone radiation for carcinoma of the uterine cervix. 3. Amebic proctosigmoiditis. Rectal granuloma is an uncommon complication of amebiasis. 4. Chronic ulcerative colitis. 5. Gonorrheal proctitis. 6. Chancre. 7. Lymphogranuloma venereum. If this causes a rectal stricture it is usually at the level of the levator ani. The Frei test is helpful in diagnosis. 8. Tuberculosis of the rectum. The author gives an excellent clinical description of these lesions, that is, their visual appearance and their feel to the palpating finger. He also discusses laboratory tests and biopsy in differential diagnosis.

SAMUEL L. IMMERMAN

PAPILLARY ADENOMAS OF THE COLON AND RECTUM: Neil W. Swinton, William A. Meissner and Wesley A. Soland, Jr. A.M.A. Arch. Int. Med., 96:544, (Oct.), 1955

Papillary adenomas (villous tumors of the colon and rectum) occur almost all below the rectosigmoid junction. They are found in an older age group than the usual adenomas and cancers. They occur mostly singly, are better seen than palpated because of their soft and velvety appearance. They are wrinkled and folded, covered with thick tenacious mucus. Villous polyps are better diagnosed by macroscopic inspection than by microscopic studies where they appear only as variants of adenomatous polyps. However, they show more a replacement of the surface epithelium by the growth than a formation of new glandular tissue. Symptoms are rectal bleeding, discharge of mucus, constipation alternating with various forms of diarrhea. Cramps and tenesmus are rare. Also there is an appreciable incidence of transformation of these tumors into cancer and a high incidence of local recurrence following snare excision and fulguration, no patients of the authors have died of lymphogenous or hematogenous metastases indicating a low grade malignant potential. Therefore, a conservative approach in the surgical management of these growths seem to be justified provided adequate clinical and pathologic follow-up studies can be maintained.

H. B. EISENSTADT

RECTAL BIOPSY AS AN AID IN THE DIAGNOSIS OF HIRSCHSPRUNG'S DISEASE: Orvar Swenson, John Herbert Fisher and H. Edward MacMahon. New England J. Med., 253:632, (13 Oct.), 1955.

There are four groups of cases in which diagnosis is difficult. 1. An inactive segment of colon beyond a colostomy. 2. When the entire colon is aganglionic. This causes a "physiologic" obstruction. 3. A short narrow segment, so low down in the rectum that the roentgenologist cannot demonstrate it. 4. Atypical symptoms such as diarrhea, without typical x-ray findings.

The rectal biopsy must be adequately performed. Under general anesthesia, with patient lying on the left side; the anus is dilated, and a one centimeter logitudinal incision is made through the mucosa on the side of the anal canal, beginning at the white line of Hilton and extending up between the columns of Morgagni. By means of proper dissection and anatomical landmarks described by the authors a segment of muscle is excised; the ganglion cells lie between the circular and longitudinal layers. In 40 cases in which this was done there was one case which required additional suturing. Multiple histological sections are carefully examined. The authors found the method extremely valuable.

SAMUEL L. IMMERMAN

CARCINOID TUMORS OF THE GASTROINTESTINAL TRACT: Merrill O. Hines, Patrick H Hanley and H. Lamar Boese. A.M.A. Arch. Int. Med., 96:500, (Oct.), 1955.

Carcinoid tumors of the gastrointestinal tract may occur anywhere from the cardia to the rectum. Rarely are they found in gallbladder, Meckel's diverticulum, nasal cavity, cervix, pancreas, perirectal region, testes, prostate, mesentery and liver. These tumors originate from the argentaffin cells in the base of the crypts of Lieberkühn. The most common site of carcinoids reported in the literature is the appendix, the second most frequent the ileum. However, in the last few years the greatest number of carcinoids have apparently been observed in the rectum. All carcinoids are potentially malignant and will produce metastases, if the patients live long enough. Carcinoids show a low grade malignancy; even persons with widespread metastases remain in relatively good health and live comfortably for a long time. The cachexia of other malignancies is absent. Carcinoids of the colon are the most malignant types causing stenosis, ulceration, gastrocolic fistula and are difficult to distinguish clinically from adenocarcinomas. On the other hand rectocarcinoids are usually quite benign.

H. B. EISENSTADT

THERAPEUTIC ASPECTS OF A WATER-BORNE OUTBREAK OF AMEBIASIS IN SOUTH BEND, INDIANA: Robert W. Sappenfield, F. R. N. Carter, Carl Culbertson, Marion M. Brooke, Fred M. Payne and William W. Frye. J.A.M.A., 159:1009, (5 Nov.), 1955.

In studying an outbreak of amebiasis occurring in a woodworking plant in South Bend, Indiana, the authors found that 51 per cent of the group sampled were infected with *Endameba histolytica*. Accordingly some 805 persons were divided into 2 groups; one group of 405 received oxytetracycline, the other group of 400 individuals received fumagillin. After one course of treatment with each drug, patients were stool tested for persistence of the parasite and if still positive were given the other drug. Comparison of the drugs showed both to be effective amebacides since a 3 to 4-month follow-up revealed absence of histolytica in over 93 per cent of people treated. Both drugs were approximately equally effective in eliminating the parasite. Complaints due to side-effects of the drugs were usually of a mild nature and tended to disappear after completion of therapy. Complaints characteristic of fumagillin were a syndrome of abdominal tenderness, dizziness and extreme weakness, a typical skin rash and gastric irritation. Complaints characteristic of oxytetracycline were diarrhea and itching and prolonged rectal irritation.

W. K. BILLINGSLEY, JR.

LIVER AND BILIARY TRACT

LIVER DISEASE IN SICKLE CELL ANEMIA—A correlation of clinical, biochemical, histologic and histochemical observations: A. Bogoch, W. G. B. Casselman, M. P. Margolis and H. L. Bockus, Am. J. Med., 19:583 (Oct.), 1955.

Clinical and biochemical studies and histologic and histochemical observations on liver tissue obtained by a needle biopsy were made on four patients with sickle cell anemia. There was one instance of hepatitis, one of hemachromatosis and two of portal cirrhosis. Hepatitis in one patient was thought to be a manifestation of the sickle cell disease per se. Focal parenchymal lesions were found in the liver during the recovery stage and it is likely that some of the necrotic lesions, when prominent and repeated, may be followed by cirrhosis as another hepatic manifestation of sickle cell anemia. Hemochromatosis in one patient was unquestionably related to multiple blood transfusions. The significance of serial liver function tests was discussed. The serum alkaline phosphatase test is of limited value as an aid in differentiating jaundice of hepatic from posthepatic origin because osseus involvement in the absence of radiologic evidence may occur in sickle cell anemia. Elevated serum amylase and lipase values were found in several instances. Because of the abdominal manifestations, the condition may be confused with acute primary pancreatitis. Histochemical studies revealed no, or only mere traces, of demonstrable lipids in the cytoplasm of the parenchymal cells.

JOHN M. MCMAHON

INFLUENCE OF THE LIVER ON BONE METABOLISM: M. Hines Roberts and Cary Sullivan. J.A.M.A. 159:1002 (5 Nov.), 1955.

Two very interesting case reports of children in whom liver disease resulted in extensive osteoporosis are presented. In one case the skeleton was normal at the beginning of the illness, but later developed osteoporosis only to subside before the patient's death of hepatocellular carcinoma. In the second case the pathology in the bones was of long standing. Therapy did not influence the basic skeletal pathology. The liver's role in the absorption of calcium, phosphorus and Vitamin D apparently was not impaired in these patients. The authors suggest that osteoporosis in these cases resulted from interference with the liver's elaboration of some unknown substance that promotes calcification or prevents decalcification in agreement with the concept of Whipple, Hansen and McQuarrie.

WM. K. BILLINGSLEY, JR.

INTRAVENOUS CHOLANGIOGRAPHY: David J. Sandweiss and Harold Fulton. J.A.M.A. 159:998 (5 Nov.), 1955.

In the study by intravenous cholangiography using Cholografin on 100 cholecystectomized patients complaining postoperatively of epigastric or right upper quadrant pain suggestive of biliary tract disease the following results obtained.

The common duct and hepatic radicles were visualized in 94 per cent of cases. Of these 36 per cent showed normal cholangiograms, 7 per cent showed stones in the common duct and 3 per cent showed dilated cystic duct stumps. The visualized common duct was measured using a diameter of 8 mm. as the upper limit of normal. By such measurements the authors found that the width of the common duct depended neither on the presence or absence of visualized stones. They also concluded that the common duct does not necessarily dilate as a compensatory mechanism following removal of the gallbladder. In 44 per cent of the cases the terminal end of the common duct failed to visualize.

WM. K. BILLINGSLEY, JR.

AMEBIC HEPATITIS: B. H. Kean. A.M.A. Arch. Int. Med., 96:667 (Nov.), 1955.

Two clinical syndromes of hepatic amebiasis have been differentiated: amebic abscess and diffuse amebic hepatitis. In order to evaluate the latter disorder, the liver of

148 persons dying of amebiasis and of several thousand persons dying of unrelated diseases, but living in an area with high incidence of amebiasis, were examined as well as the liver biopsies performed in 50 persons with the clinical diagnosis of diffuse amebic hepatitis. No diffuse hepatic disease caused by amebae could be demonstrated. These results correspond with those of other investigators in Singapore, South Africa and Chile who failed to find diffuse amebic hepatitis in numerous biopsies as well as autopsies. The clinical diagnosis of this condition depends on the evidence of past or present intestinal amebiasis, of liver dysfunction in the absence of demonstrable localizing liver abscess, and on the therapeutic success with emetine and chloroquine. Signs and symptoms consist of elevation of the right hemidiaphragm, hepatomegaly, hepatic tenderness, jaundice and abnormal liver function. The pathological findings in some of these cases were nonspecific pyogenic liver abscess, nonrecognized amebic abscess, Laennec's cirrhosis, cancer of the liver and healed virus hepatitis. However, in the majority of cases where no hepatic abnormalities could be found, a nonspecific, toxic reaction or a sensitization process might be postulated, similar to those seen in association with ulcerative colitis, diverticulitis and other colon diseases. More often, the clinical findings are simply due to severe intestinal amebiasis with ulceration, perforation, malnutrition, toxemia and septicemia.

H. B. EISENSTADT

CIRRHOSIS OF THE LIVER WITH PROLONGED SODIUM RESTRICTIONS: Charles S. Davidson. J.A.M.A. 159:1257 (26 Nov.), 1955.

Based on the premise that sodium restriction, when continuous and of a sufficient degree, will control ascites formation in cirrhotics the author subjected 30 patients with cirrhosis to an otherwise adequate diet containing approximately 200 mg. of sodium per day for periods ranging from a few weeks to two years.

The response of these patients to this routine was of three kinds. Group 1 (4 patients) had prompt diuresis after several days on the routine and became ascites free. Group 2 (14 patients) were maintained with ascites and edema but without paracentesis for from 3-16 months. Gradually during this time ascites and edema lessened. Improvement in liver function was also frequently noted. Group 3 (12 patients) failed to lose ascites although ascites formation ceased in every case.

In spite of the above results, follow-up observation of these cases showed that the problems of chronic alcoholism and hepatic coma become the limiting factors in recovery and rehabilitation from cirrhosis of the liver.

WM. K. BILLINGSLEY, JR.

ACUTE FATTY METAMORPHOSIS OF THE LIVER ASSOCIATED WITH PREGNANCY: William B. Ober, Philip M. LeCompte. Am. J. Med., 19:743 (Nov.), 1955.

Acute yellow atrophy of the liver used to be listed among the toxemias of pregnancy until it was recognized that most of such cases were merely epidemic virus hepatitis taking a fulminant course during the vulnerable stage of pregnancy. Three cases of fatal jaundice in the last trimester of pregnancy are reported that are clinically indistinguishable from such fulminating virus hepatitis but readily separated by liver biopsy or by autopsy. They show an extensive centrilobular fatty metamorphosis without any necrosis of the liver cells and with only minimal infiltration of inflammatory cells. These hepatic abnormalities have been described by Sheehan as "obstetric acute yellow atrophy" and point more to an endo- or exotoxin than to an infectious causative agent. They might be associated with fatty degeneration of the renal tubules and have been produced by poisoning with ethionine, the competitive metabolite of methionine. Clinical diagnosis can only be made with liver biopsy. Vigorous therapy with high protein, high vitamin, fat-free diet, lipotropic agents and interruption of pregnancy is indicated.

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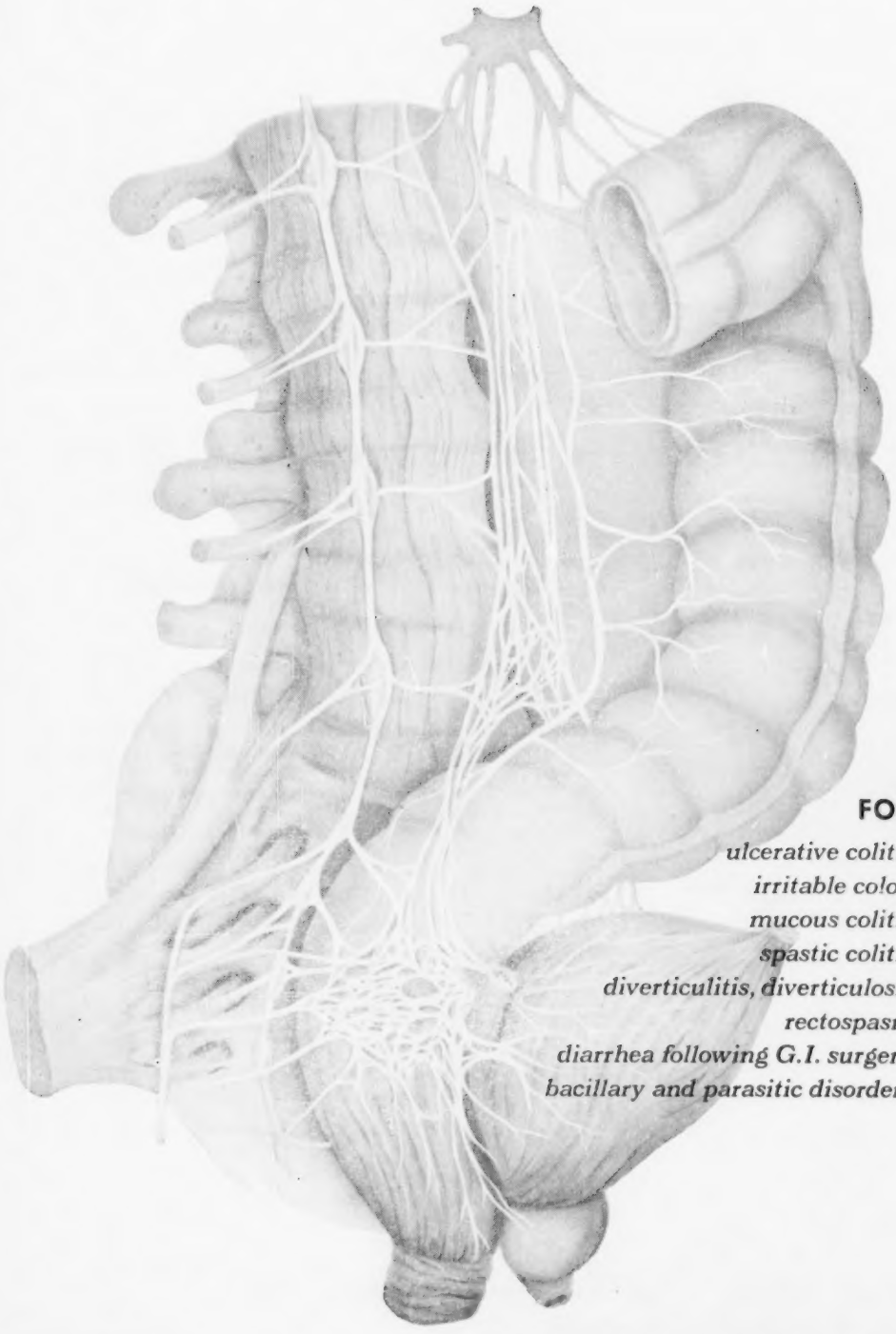

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1. Balfour, D. C., Jr.: Am. J. Gastroenterol. 22:181, 1954. 2. Burke, J. O., et al.: Internat. Rec. Med. & Gen. Practice Clin. 167:587, 1954. 3. Sternberg, S. D., and Greenblatt, I. J.: Ann. Allergy 9:190 1951.

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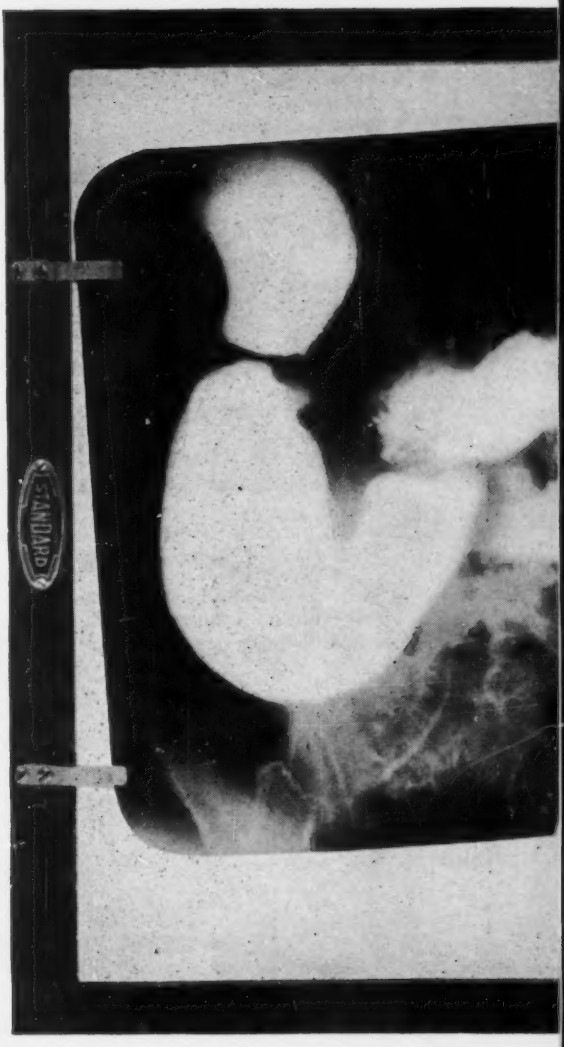

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1. Kramer, P.: Med. Clin. North America, 39:1381, Sept. 1955.
2. Morrison, Samuel: Am. J. Gastroenterology 22:309 (1954).
3. Rossett, N. E., Rice, M. L., Jr., Gastroenterology 26:490 (1954).

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1. Russ, J.D.: Personal communication.

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